Challenges of Program Implementation in a Managed Care Environment: A Case Study in Measuring Medication Persistence

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ABSTRACT

OBJECTIVE: To describe the challenges of implementing a disease management program in a managed care environment.

SUMMARY: A key element in the successful management of depression is ensuring persistent consumption of medication throughout the duration of a standard course of therapy. However, treating physicians rarely have easy access to the exact records necessary to determine medication persistence. Prescription claims databases do contain this information. Properly identifying problem consumption patterns from these data is one of the most valuable services that managed care pharmacists can provide in a disease management program. The experiences of Aetna Inc. in implementing a depression management program illustrate some of the most important factors to be considered when designing a program: obtaining approval from senior management, measuring baseline performance before program initiation, selecting plan members and physicians based on patterns of consumption in prescription claims data, and quantifying effectiveness.

CONCLUSION: A visual representation of prescription refill dates and quantities available in prescription claims databases allowed member physicians to determine, at a glance, each patient's medication persistence. Such representations of data are valuable for helping identify problem consumption patterns that require further analysis, such as noncontinuous treatment, low usage, and non-persistence. However, such data are not recommended for use in a vacuum—that excludes considerations such as therapeutic indication and environment.

KEYWORDS: Pharmacy, Disease management, Benchmarking, Managed care, Patient compliance

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A key element in the successful management of depression is ensuring persistent consumption of medication throughout the duration of a standard course of therapy.^{1,2} This is also one of the most difficult elements for treating physicians to track because they rarely have easy access to exact records of prescription refill dates and quantities. Prescription claims databases do contain this information; properly identifying problem consumption patterns from these data is one of the most valuable services that managed care pharmacists can provide in a disease management program. This applies not only to depression but also to cardiovascular disease, diabetes, asthma, and a host of other chronic conditions that are frequently the subject of disease management.

Aetna Inc. included for physicians a graphical representation of their patients' medication persistence as part of a depression management program. Figure 1 shows part of the information that was presented to physicians in this program. The graph shows bars on a calendar representing the time period during which each patient was taking medication according to prescription claims data. This arrangement allowed physicians to determine, at a glance, which patients had been receiving medication for the period of time recommended in treatment guidelines.

Implementing such a program requires several steps with which all managed care pharmacists are familiar. The Aetna program will be used as a case study to illustrate some of the most important factors to be considered when designing a program: obtaining approval from senior management, measuring baseline performance prior to program initiation, selecting plan members and physicians based on patterns of consumption in prescription claims data, and quantifying effectiveness by measuring results.

Plan Member Populations and Medications Examined

It is important, during the design phase of a disease management program, for the development team to discuss the specific characteristics of the member population to be included. These characteristics will vary depending on the specifics of the disease state targeted. For example, with depression programs, there should be some consideration about whether pediatric patients should be included, because of the ambiguity within the medical literature regarding the most appropriate therapy for these patients.³ These members were not included in the Aetna program.

Another point to be discussed is whether to include members under the care of a specialist. It may be argued that such members have more complex disease states and that treating psychiatrists are already very familiar with the standard treatment guidelines, which they adapt to the more unusual conditions of their individual patients. But they do still face the problem of lack of easy access to prescription refill records and may find concise information on

FIGURE 1 Days of Antidepressant Treatment Over Time

This is an example of the graphical representation of medication persistence physicians received from Aetna Inc. as part of a depression management program. The graph shows bars on a calendar representing the time period during which each patient was taking medication according to prescription claims data.

this subject very useful. These patients were included in the Aetna program.

Antidepressant medications are indicated for several conditions other than depression, including obsessive-compulsive disorder, panic disorder, anxiety conditions, and posttraumatic stress disorder.⁴ For example, if tricyclic antidepressants (TCAs) are included in the program, this list of indications may include chronic pain, urinary incontinence, and several other conditions. Likewise, if trazodone is included, then insomnia may be the most relevant indication. It would be confusing to the member and physician if educational materials were sent on depression treatment for patients who were prescribed the medication for another condition. While this problem of misidentification is a general limitation of algorithm-driven programs, the problem can be minimized by combining pharmacy claims data with medical

claims data. If this is not available, then the list of antidepressant drugs used as triggers of member identification should be limited to only those that are not frequently prescribed for conditions other than depression.

Since medical claims data was available in the Aetna program, only the members with an *International Classification of Diseases, Ninth Revision* (ICD-9) diagnosis code specific to depression were included (ICD-9 codes 296.2, 296.3, 300.4, 301.12, 311). If the data available are restricted to pharmacy claims, then it is important for the cover letter or educational materials to include a disclaimer indicating that some of the patients identified by the program may be taking the medication for conditions other than depression.

If diagnosis data are not available, it may also be wise to exclude members who have no history of receiving a selective serotonin reuptake inhibitor or selective norepinephrine uptake

FIGURE 2 Potential Effects of Time on Claims Data
(Percentage of Members Persistent at 6 Months)**A. Baseline With No Pattern Over Time** **B. Baseline With Trend Over Time** **C. Baseline With Seasonal Trend**

Random variation in the percentage of the same members over 6 months of treatment may demonstrate no overall pattern (A), but if data show a steady change over time (B), that change needs to be identified. One example is with the trend observed in C, which appears to indicate a reduction in the duration of treatment. More careful consideration of facts such as that the programs began in August or September and that the trend was seen in northern regions but not in southern regions indicated that the patients starting antidepressant treatment in the autumn and winter may have been suffering from seasonal affective disorder and may have discontinued their medication early once spring brought more hours of daylight.

inhibitor. Once members have been identified as being treated for depression, however, other medications such as TCAs or trazodone should be included in the overall examination of the patient's pattern of consumption. If the claim is made that the member was not taking antidepressant medications during a

specific time period, and the treating physician knows that the member was in fact taking a tricyclic, then the overall credibility of the information may be questioned.

Measuring Baseline Performance

Obtaining a baseline measurement of the number of plan members who receive a full course of therapy and maintain adequate medication persistence, before a program is implemented, is important both in selling the program to senior management and in determining whether the program was effective. Factors that must be considered when measuring this baseline include changes in overall consumption patterns over time, changes based on the location of plan membership, and changes based on the drug mix being consumed.

Figure 2 depicts graphical representations of various effects of time on claims data. In 2A, there is some random variation in the percentage of members who remained persistent for 6 months of treatment, depending on the month at which the data were measured, but there is no discernable overall pattern. If the data were to show instead a steady change over time, as in the hypothetical pattern shown in 2B, then that change must be accounted for. If the program were implemented in December in this case, it would be very difficult to claim that the increase seen from December through the following July was due to the program, rather than being a continuation of the underlying trend seen before.

If such a pattern were to be seen, then it would be important to determine the cause in order to decide whether that underlying trend would be expected to continue during the period following the intervention. Ideally, some subset of members to whom the program did not apply (for reasons such as plan design or plan sponsor "no-touch" requests) should be used as a control group. A fitted trend, such as the Hodrick-Prescott filter, can then be calculated for the control group; if this trend matches for the study and control groups prior to the intervention, then the trend for the control group after the intervention can be removed from the study group.

While the hypothetical pattern seen in 2B would be very unlikely in real data, the pattern in 2C is more likely, and was, in fact, typical of certain metropolitan areas at more northern latitudes within the Aetna program. Cities at southern latitudes did not display this pattern, leading to the hypothesis that some of the patients starting antidepressant treatment in the autumn and winter may have been suffering from seasonal affective disorder and may have discontinued their medication early once spring brought more hours of daylight. In these cases, a program started in August or September may artificially appear to actually reduce duration of treatment, a fact that must be accounted for in determining program effectiveness.

In this case, it would be important to compare postintervention results with preintervention results from only the same time period during prior years, not with the time period immediately

before the intervention. If enough data is available to use autoregressive time-series statistical techniques, then seasonality can be accounted for by using a model such as ARIMA (AutoRegressive Integrated Moving Average), which allows for seasonal adjustment, to project a forecast of what the results would have been without the intervention. This forecast can then be compared with the actual postintervention data to determine whether actual results fell outside the confidence interval of the predicted results.⁵ This approach does require a substantial amount of data prior to the intervention (generally at least 5 years, during which there have been no major shifts in standard treatment for the condition being studied); it also is limited to results that are expected to appear quite soon after the intervention because the confidence interval for the predicted results widens substantially for each successive time period after the intervention.

Similarly, if there were changes in the location of the member population during the program period or the baseline measurement period, then it is possible that those changes could skew the results. This could happen, for instance, if the plan underwent a merger or acquired a new client that brought into the program a large number of new members in a city where membership previously had been low. Local medical practices may affect treatment patterns in different metropolitan areas, so if there was a substantial change in membership, then that possibility should be accounted for in the data analysis by restricting postintervention data to the same populations that received the intervention and using multivariate statistical techniques that include geography in the regression model.

Changes in the drug mix used for treatment may also potentially skew the results. It is possible that certain drugs are more frequently associated with longer duration of treatment than other drugs within the same therapeutic category.^{6,7} If a change in the drug mix consumed by the population were to occur (e.g., due to introduction of new medications to the market, supply difficulties by a particular manufacturer, or changes in the health plan formulary or policy), then that change should be explained.

Measuring Persistence

Converting pharmacy claims data into useful information on medication persistence requires the dedication of computer programming resources, which are typically scarce within any organization. This challenge to program implementation may appear extremely difficult to overcome. Many desktop applications, however, include access to a programming language that is both powerful enough to handle this task and safe enough to fit within corporate security guidelines designed to prevent corruption of network data by unauthorized computer programs. Microsoft Visual Basic for Applications, which is available within the standard desktop implementations of Microsoft Excel and Microsoft Access programs, was the language used for the Aetna program. Managed care pharmacists who are reasonably astute in computer usage may well be able to teach themselves enough

FIGURE 3 Rewriting Prescription Claims to Measure Persistence Gap

A.

Member ID	Drug	Date	Qty.	Days Supply
AABBCCDDI	Fluoxetine 20 mg	01/01/2005	10	10
AABBCCDDI	Fluoxetine 20 mg	01/14/2005	10	10

B.

Medication?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y					Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24			

This is an example of the graphical representation of medication persistence physicians received from Aetna Inc. as part of a depression management program. The top (A) of this figure represents how pharmacy claims data appears. The bottom (B) is a calendar representation of the days since the patient began taking medication.

about embedded languages to develop such an application. Because of the need to accomplish this in order to implement any medication persistence program, some time will be spent here discussing the technical details of how it is done.

Figure 3A shows typical prescription claims data, and 3B shows these data converted into a format useful for measuring persistence. Usually this format is placed within the programming data structure known as an array, although some programmers may prefer a linked list or other data structure. For purposes of this figure, it is perhaps easiest to think of the 2 rows of data in 3B as 2 rows in a spreadsheet. The first box in the top row, which contains a Y, would correspond to cell A1 of the spreadsheet. The Y refers to the fact that, yes, this member did have medication available on the date referred to by this cell. Row 2 labels the days for each cell in row 1. Thus, cell B1 corresponds to 01/01/2005, the first day in this member's drug history, and cells A1 and B1, taken together, indicate that on this date the member had drug available. Since the prescription filled on this date was for a 10-day supply, the first 10 columns of row 1 all contain a Y. The next prescription was filled on 01/14/2005, and was also for a 10-day supply, so the cells corresponding to this date are marked with a Y. This leaves a gap during which the member had no medication available for days 11, 12, and 13. Much of the art of measuring persistence lies in interpreting this gap and specifically assessing whether its duration indicates an interruption in medication usage to an extent representing nonadherence.

While the Yes-No approach illustrated in Figure 3 is useful, it accounts neither for the possibility of insufficient dosage nor for the handling of member histories that include multiple types of antidepressant medication. Consider Figure 4. In 4A the member has 2 different types of medication, fluoxetine and amitriptyline, with 2 different strengths of amitriptyline. In 4B, this history is placed onto the spreadsheet, with one row representing each drug and strength (or into a 2-dimensional array, with each row of the array representing one drug and strength). Rather than a binary Y-N to designate if the drug is available or is not available, as demonstrated in Figure 3, each cell now contains a number

FIGURE 4 Measuring Persistence Gap With Multiple Medications

A.	Member ID	Drug	Date	Qty.	Days Supply
	AABBCDD1	Amitriptyline 10 mg	01/01/2005	60	30
	AABBCDD1	Amitriptyline 25 mg	01/01/2005	20	10
	AABBCDD1	Amitriptyline 25 mg	01/14/2005	20	10
	AABBCDD1	Fluoxetine 10 mg	01/13/2005	10	10

B.	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Amitryp 10 mg	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	Amitryp 25 mg	2	2	2	2	2	2	2	2	2	0	0	0	2	2	2	2	2	2	2	2	2	2	2	2
	Fluox 10 mg	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1

C.	Drug	% Ped. Min. Dose	% Adult Min. Dose	% Ger. Min. Dose
	Amitriptyline 10 mg	0.333	0.2	0.333
	Amitriptyline 25 mg	0.833	0.5	0.833
	Fluoxetine 10 mg	1	1	1

D.	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Amitryp 10 mg	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4	.4
	Amitryp 25 mg	1	1	1	1	1	1	1	1	1	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1
	Fluox 10 mg	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1

E.	Pet Min Dose	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4
	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24

(A) Medical claims data showing history is placed onto the (B) spreadsheet (or into a similar 2-dimensional array), with one row of the spreadsheet or array representing each drug and strength. Each cell in the row of the spreadsheet contains a number corresponding to the number of capsules of the particular drug available on the particular date. An additional table (C) was developed to translate this into useful information on persistence. All of the cells in the column corresponding to a single day were multiplied by the correct dose from this table and the result was placed into another array on the spreadsheet (D). All of the cells corresponding to a single day in this array were then summed into (E), the final array. The gap days being measured were then considered to be all days in this final array having a total of less than one.

FIGURE 5 Incorrect Days Supply

Member ID	Drug	Date	Qty.	Days Supply
AABBCDD1	Amitriptyline 10 mg	01/01/2005	60	2
AABBCDD1	Amitriptyline 25 mg	01/01/2005	20	2
AABBCDD1	Amitriptyline 25 mg	01/14/2005	20	2
AABBCDD1	Fluoxetine 10 mg	01/13/2005	10	2

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Amitryp 10 mg	30	30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Amitryp 25 mg	10	10	0	0	0	0	0	0	0	0	0	0	0	10	10	0	0	0	0	0	0	0	0	0
Fluox 10 mg	0	0	0	0	0	0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0

Drug	% Ped. Min. Dose	% Adult Min. Dose	% Ger. Min. Dose
Amitriptyline 10 mg	0.333	0.2	0.333
Amitriptyline 25 mg	0.833	0.5	0.833
Fluoxetine 10 mg	1	1	1

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Amitryp 10 mg	6	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Amitryp 25 mg	5	5	0	0	0	0	0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0
Fluox 10 mg	0	0	0	0	0	0	0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0

Pct Min Dose	11	11	0	0	0	0	0	0	0	0	0	0	0	5	10	5	0	0	0	0	0	0	0	0	0
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	

Here, when the prescriptions were originally filled, the days supplies were entered incorrectly as a 2-day supply for each claim. The algorithm then dutifully performed the same calculations as described in Figure 4, with the resulting assumption that on days 1 and 2, the member consumed 1,100% of the standard adult minimum dose, with a gap extending from days 3 through 12. To correct this, you can include a table of standard daily dosages within the computer program or clean up the data before using it by dividing the quantity dispensed by the days supply, then sort the results in descending order and manually examine the top claims.

corresponding to the number of doses of the particular drug available on the particular date. The member received 60 tablets of amitriptyline 10 mg on 01/01/2005, which was a 30-day supply; 60 is divided by 30 to yield 2 tablets per day, so 2 was placed into the cells in row 1 for each of the 30 days from 01/01/2005 through 01/30/2005.

To translate this into useful information on persistence, a table such as that shown in Figure 4C was developed. The medical literature indicated that, for an adult, a daily dose of 50 mg of amitriptyline is required to effectively treat depression, so one tablet of 10 mg would represent 20% of the minimum adult dose. The 2 tablets in row 1 of Figure 4B were therefore multiplied by 0.2 and placed into the appropriate cells in the array in Figure 4D. This was repeated for each drug in the member's history. All of the cells in each column corresponding to a single day were summed into the final array shown in Figure 4E. The gap days being measured were then considered to be all days having a total of less than 1 in the final array.

Sometimes, using this approach will present a data cleanup problem that must be corrected. In Figure 5, when the prescriptions were originally filled, the days' supplies were entered incorrectly as a 2-day supply for each claim. The algorithm then dutifully performed the same calculations as shown in Figure 4, with the resulting assumption that on days 1 and 2, the member consumed 1,100% of the standard adult minimum dose, with a gap extending from days 3 through 12. Such situations are rare, but if the population being examined includes more than a few thousand members, the problem is bound to come up at least a few times.

It is possible to include a table of standard daily dosages in the computer program in order to correct this, but it is simpler to clean up the data before using them. Divide the quantity dispensed by the days supply, then sort the results in descending order and manually examine the top claims. In general, the human eye can spot problem claims better than a computer program, and the day supply field can be corrected by hand. The problem is rare enough that this approach is practical even when analyzing very large datasets.

Once the final array has been produced indicating which days in the member's history are considered treatment gaps, then it is necessary to decide what patterns of treatment gaps constitute inadequate persistence. A useful overview of this topic can be found in a 2005 study by Sikka and colleagues.⁸ They reported no standard in the medication persistence literature, with permissible gaps ranging from 15 days to 120 days.

Some studies look only at individual gaps, with a patient considered nonpersistent if any single gap exceeds the permissible number of days. This approach does not allow for the cumulative effect of multiple gaps that are close together in time. For instance, a member may receive a 30-day supply on June 1, then another 30-day supply on July 30, and another on September 25. If a 30-day permissible gap is used, then none of the gaps exceeds the

limit. Actual consumption behavior for this member cannot be known, but it is known that the average daily consumption is considerably lower than the dose indicated by the days supply. Thus, it is very likely that the patient is missing doses of the medication several days per week. If the resultant consumption is less than the minimum indicated for the drug in Figure 4C, then the member cannot be considered as having persistent consumption. Even if the consumption level is above the minimum effective dose, it is beneficial to inform the treating physician that consumption may be lower than that indicated by the dosage instructions. Doing this requires that the consumption algorithm include some mechanism for combining multiple gaps to determine the cumulative effect.

One goal of the Aetna program was to improve plan performance in the Health Plan Employer Data and Information Set (HEDIS) established by the National Committee for Quality Assurance. HEDIS measurement standards include the definition that antidepressant treatment is not considered continuous if the cumulative gap in treatment days exceeds a total of 30 days during the acute phase (the first 114 days of treatment) or 51 days during the continuation phase (the first 231 days of treatment).⁹ This is the definition that was used for the Aetna program.

From the perspective of the HEDIS definition, and of most studies reported in the medical literature, the most important time period starts on the day that treatment is initiated and continues until a gap indicates that the patient is no longer taking medication in a persistent manner.⁸ This is also the most important time period to consider when measuring the population baseline and program effectiveness. In these applications of the information, once a patient has been classified as nonpersistent, that person is no longer considered in the analysis, even if he or she restarts treatment and remains compliant. But when reporting individual patient histories to treating physicians, it is just as important to consider recent compliance as it is to consider compliance during the first days after treatment was started. It is not appropriate to state that a patient is nonpersistent when, in fact, that patient's recent behavior has been persistent. What period of time should be considered recent behavior? For the Aetna program, the time period was counted backwards, starting on the last day that had a supply of medication, then moving back in time until the cumulative gap days exceeded 51 days if total duration was greater than 114 days, or 30 gap days if total duration was 114 days or less (for baseline and program effectiveness measurements, the normal forward progression was used).

Measuring Program Effectiveness

In some studies of programs designed to improve persistence with chronic medications, the behavior of a member during the pre-study period can be compared with the behavior of the same member during the poststudy period, providing an effective control group. But to use this methodology (i.e., the "patient-as-their-own-control" design), the level of persistence for each

FIGURE 6 Patients of AMM Physicians, Newly Starting Antidepressant Medications, Preintervention and Postintervention

Kaplan-Meier survival curves were constructed for patients treated by program physicians after the intervention (solid line) and patients treated by the same physicians before the intervention (dotted line). A Cox proportional hazards model was used to compare these curves—controlling for age, gender, and the presence of comorbid conditions—and demonstrated a modest but statistically significant improvement in persistence with antidepressant medications.

member in the poststudy period must be independent of the level of persistence for that member during the prestudy period.¹⁰ This is not the case with antidepressants because it is normal for a patient to complete a course of therapy and then discontinue the medication. It is possible to create a control group by deliberately withholding a set of members from the program for that purpose, but this is not generally considered appropriate. The approach used in the Aetna study was to compare prestudy and poststudy populations of all members being treated by physicians who were included in the educational portion of the intervention. The assumption was that physicians contacted during the program stress persistence more often with patients who were newly started on antidepressant medications, shortly after they received educational information. Figure 6 illustrates this assumption. A comparison of patients treated by program physicians before and after intervention showed a modest but statistically significant improvement in persistence with antidepressant medications for the population treated by program physicians after the intervention (as determined by a Cox proportional hazards model).

Conclusions

Ensuring medication persistence throughout a standard course of therapy is critical to the successful management of depression. Prescription claims databases contain the information, such as exact records of prescription refill dates and quantities, necessary

to determine medication persistence. Treating physicians rarely have access to these data and may not know the intricacies of interpreting it. Properly identifying problem consumption patterns from these data is one of the most valuable services that managed care pharmacists can provide in a disease management program. A visual representation of prescription claims database information can be tailored to help member physicians determine, at a glance, each patient's medication persistence. Such representations of data are valuable for helping identify problem consumption patterns that require further analysis, such as treatment that is not continuous; low usage; and nonpersistence. However, such data are not recommended for use in a vacuum—that excludes considerations such as therapeutic indication and environment.

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