Antidepressant Medication Adherence via Interactive Voice Response Telephone Calls

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Objectives: Outpatients given antidepressants discontinue treatment at a high rate during the first few months. We evaluated the effectiveness of Highmark's use of interactive voice response (IVR) to improve antidepressant medication adherence.

Study Design: Quasi-experimental cohort intervention study.

Methods: We placed 39,020 members newly given antidepressant medication into 3 intervention groups based on results of interactive voice response (IVR) call 1 month post-prescription: (1) not reached; (2) reached but not transferred to depression management consultant (DMC); and (3) reached and transferred to DMC. We evaluated medication adherence based on the Healthcare Effectiveness Data and Information Set effective acute phase (3 months) and continuation phase (6 months) treatment outcomes using member claims data. We used generalized estimating equations to model intervention effectiveness on medication adherence.

Results: Adherence increased markedly with age group, with members older than 65 years having a 5.11-fold higher odds (P <.0001) of compliance than the baseline group aged 18 to 24 years. In models adjusted for time, month of intervention, and drug, the odds of compliance for groups (3) and (2) relative to group (1) were 1.34 (P = .009) and 1.19 (P <.001), respectively. In models also adjusted for age group, the group (3) and (2) odds decreased to 1.00 and 1.03 and were not statistically significant.

Conclusions: We found that IVR calls had little impact on antidepressant medication adherence rates. Adherence rates increased markedly with increasing age in each intervention group, suggesting that other intervention strategies to improve adherence should focus on the younger segment of the patient population.

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For author information and disclosures, see end of text.

Adherence to antidepressant therapy is essential for a positive patient outcome, and guidelines issued by the American Psychiatric Association recommend that patients continue their antidepressant medication for a period of at least 4 to 9 months post–depression symptom resolution in order to prevent relapse.[1] However, research has shown that nearly 50% of patients given an antidepressant as an outpatient discontinue medication treatment during the first month. Upon analysis at the 3-month time frame after antidepressant therapy has begun, the discontinuation rate can reach 68%, depending on the population and the specific antidepressant prescribed.[2]

Health plans across the country have attempted many intervention strategies to improve antidepressant adherence among their membership. These strategies have been reviewed and summarized by several authors.[3-6] Adherence strategies include: (1) physician and pharmacy notifications, (2) case management outreach, (3) physician education, (4) behavioral health consultation for primary care providers, (5) educational mailings, and (6) interactive voice response (IVR) technology. IVR is a technology that allows a computer to detect voice and keypad inputs, typically used to automate dialogue during a phone call. IVR consists of a dialogue between a human user and a computer. The computer prompts the user with either prerecorded prompts or synthesized speech and the user can respond by some combination of voice, touch-tone keys, and auxiliary input devices.

IVR technology has been associated with favorable health outcomes in a variety of therapeutic areas (eg, diabetes, pain management, hypertension) and health behaviors (eg, smoking cessation, physical activity), although equivalent as well as negative findings have also been reported.[7-15] IVR has also been shown to improve medication adherence for certain medications such as oral anticoagulants[16] and statins.[17,18] Limited research has been conducted, however, on the effectiveness of IVR technology on antidepressant medication adherence per se. For example, we identified only 1 published study, a randomized controlled clinical trial, which found IVR technology did not improve antidepressant medication adherence.[19] Mundt et al[20] used IVR to obtain clinical assessment data in a study of the impact of a time-phased patient education program on antidepressant medication compliance, but IVR was not an explicit component of the intervention. Kaiser Permanente, in collaboration with the National Institute of Mental Health, is currently recruiting adult sub-

jects with depression/anxiety diagnoses into a randomized controlled clinical trial of antidepressant adherence via IVR (http://clinicaltrials.gov/ct2/show/NCT01188135).

This article will focus on the effectiveness of a health plan's use of IVR to improve antidepressant medication adherence. Highmark Inc (Highmark), a leading health plan based in Pittsburgh, Pennsylvania, has been using IVR technology since 2009 to generate educational outreach calls to its commercial and Medicare Advantage members 18 years and older who have been newly given an antidepressant. The goal of the outreach is to encourage antidepressant medication adherence by providing education and resources to health plan members. Eliza Corporation, a health engagement management company in Danvers, Massachusetts, whose solutions include IVR outreach, was used for the IVR outreach to this population.

Take-Away Points

Evaluations of the effectiveness of intervention programs must carefully account for potential confounding by 1 of more study factors including age group, which may be related to both intervention group and intervention outcome.

■ Our age-adjusted evaluation of the effectiveness of interactive voice response (IVR) calls as an intervention strategy for improving antidepressant medication adherence found that IVR calls had little impact on antidepressant medication adherence rates.

■ We found adherence rates generally increased markedly with increasing age, suggesting that other intervention strategies to improve adherence should focus on the younger segment of the patient population.

METHODS

IVR Call Protocol

Before implementation of IVR calls, Highmark's Behavioral Health Quality Improvement Committee (BHQIC) discussed the pros and cons of using IVR with depressed members. The BHQIC consisted of primary care physicians (PCPs), psychiatrists, psychologists, licensed clinical social workers, and registered nurses. BHQIC members were hesitant to implement an IVR call initiative due to the sensitivity of a depression diagnosis; however, they acknowledged the benefit of educating several thousand additional members by using IVR outreach versus telephonic case management outreach. The actual IVR call language was also reviewed by many other Highmark departments, including the law department, to avoid potential complications. At the conclusion of the IVR call initiative, Highmark did not receive any complaints about the script language; however, a few members requested no future IVR calls for any diagnosis. Highmark attributes the lack of compliance to the time spent crafting the script to ensure confidentiality and accuracy.

Prescribing practitioners were not engaged in the IVR call initiative, as the year before implementation, Highmark conducted a networkwide initiative for PCPs including a behavioral health tool kit mailing. The tool kit included education on various behavioral health diagnoses, including depression. It also included a Highmark Depression Management Program (DMP) referral form, a patient educational depression brochure, and various screening tools. Highmark felt that the PCP tool kit mailing provided sufficient education and resources for the PCP at that time. However, shortly after the tool kit mailing, Highmark determined that member education regarding antidepressant medications remained a barrier to adherence, thus the initiation of the IVR calls.

One prerecorded script was used for this IVR call initiative, which occurred as a cold call, without prior notification. The script was reviewed extensively by the BHQIC to assure that sufficient information was provided regarding antidepressants. The BHQIC also reviewed and minimized the script length with the goal of increasing the number of members who would listen to the entire call and not hang up. The member was introduced to the call by stating that Highmark was calling with an important health message. The call did not state anything initially about the member being given an antidepressant, in an effort to protect confidentiality. Later in the script, the call identifies the prescribed antidepressant, but states it "may" have been prescribed for the member, which was another strategy to protect confidentiality. Detailed information was provided on antidepressant side effects and the member was highly encouraged to speak to their physician regarding those side effects. In addition, the call provided an opportunity for the member to be transferred to the DMP at the beginning of the call to speak to a case manager versus listening to the entire call. To maximize participation, IVR calls were attempted several times until a person was reached or there was the ability to leave a Health Insurance Portability and Accountability Act–compliant message on an answering machine or with another person in the household. The member had the ability to call back and receive the message as well.

Highmark received little feedback on what the member experienced during the IVR call, which included an open member comments section. And although the member had the opportunity to speak with someone in the DMP, the case managers focused on the reason for the transfer at that time and were not prompted to gather member input on the actual IVR call experience.

Intervention Study Design

Members eligible for the IVR phone calls were those who had been newly given an antidepressant medication from No-

■ **Figure 1.** IVR Phone Call Flow Diagram
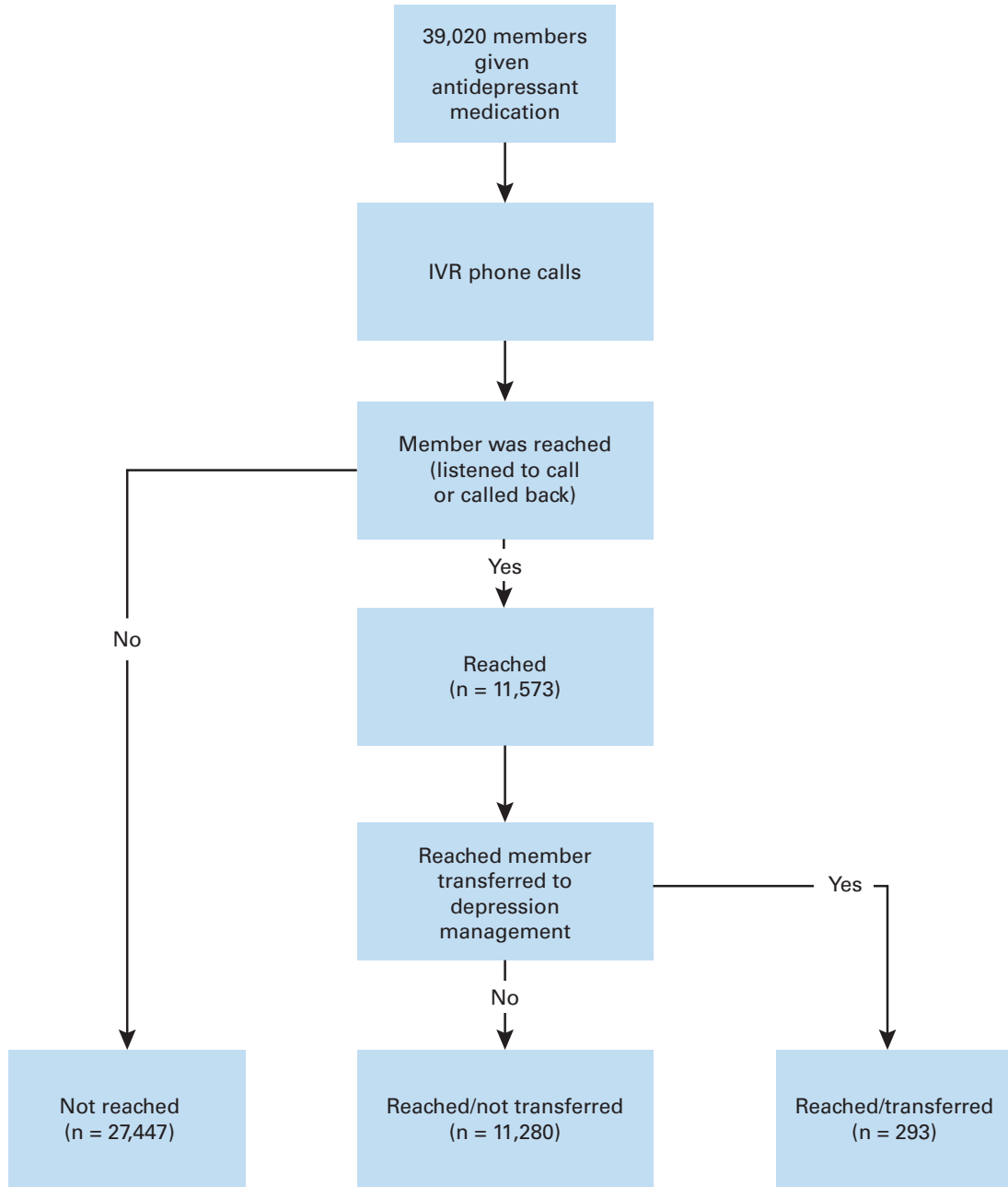
IVR indicates interactive voice response.

vember 2008 to November 2009. The IVR calls were placed December 2008 through December 2009. The IVR call process entailed the following: (1) calls were placed to members 1 month after being given an antidepressant; (2) if a member was reached, they had the opportunity to listen to the call and to be transferred to the Highmark DMP; and (3) if a member was unreachable, a message was left for the member asking them to call back to hear the important health message.

Data on medication adherence were collected from mem-

ber claims for calendar year 2009 and the first half of calendar year 2010. To evaluate the impact of the IVR calls on antidepressant medication adherence, Highmark chose the National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS, a registered trademark of the NCQA) as its measurement tool. This tool is used by more than 90% of America's health plans to measure performance on important dimensions of care and service.

Based on the results of the automated call and for the purpose of this analysis, members were divided a posteriori into 3 intervention groups. These groups were defined to indicate the degree to which the member was engaged in the phone call or depression management process. The 3 groups, in increasing levels of engagement, are: (1) not reached, (2) reached/not transferred, and (3) reached/transferred. If a member did not listen to the IVR call or did not return a phone call in response to a message, he or she was considered to be not reached. If a member chose to continue with the call or if a message was left and the member called back, the member was reached. If the member was reached and declined to be transferred to a depression management consultant, the member was reached/not transferred. If the member was reached and asked to be transferred to a depression management consultant, the member was reached/transferred. Members were encouraged to transfer to a depression management consultant for any questions or to discuss concerns such as medication cost or possible side effects.

The 2 HEDIS outcomes of interest involving antidepressant medication management in this study are effective acute phase and effective continuation phase treatment. Effective acute phase treatment is defined as the percentage of newly diagnosed and treated members who remained on an antidepressant medication for at least 12 weeks (3 months). Effective continuation phase treatment is the percentage of newly diagnosed and treated members who remained on an antidepressant medication for at least 6 months. The goal of the study is to compare adherence rates by the 3 intervention groups (not reached, reached/not transferred, reached/transferred) to determine if the IVR calls affect antidepressant medication adherence rates.

Member level information available from claims data was limited, but included: age (at intervention), region (central Pennsylvania, western Pennsylvania, or other), sex, metropolitan statistical area (MSA) type (urban, rural, or suburban), date of intervention, drug prescribed, and the acute and continuation medication adherence.

Statistical Analysis

We compared the distribution of member characteristic variables across the 3 phone call status groups using the χ^2 test for the categorical variables. For the continuous age variable, we used the Kruskal-Wallis test to test the hypothesis that age was equal in the 3 groups. The outcome variable of interest was adherence (a member was adherent if he or she took their medication). Adherence was measured at 2 time periods per member: acute (3 months) and continuation (6 months). Because the acute and continuation phase adherence outcomes are correlated (the adherence was assessed twice per member,

ie, repeated measures), we used generalized estimating equations (GEEs) to test for effectiveness of the intervention. The GEE model was specified with the binomial distribution and the logit link function, because a member was either adherent or not adherent. The correlation of repeated measurements was specified using an exchangeable correlation matrix structure. The GEE modeling also allowed for adjustment of other member characteristics such as age and sex. All analyses were performed in Stata 11 (StataCorp, College Station, Texas).[21]

RESULTS

IVR Phone Call Status

Figure 1 shows the flow diagram for the IVR intervention. For the period December 2008 to December 2009, there were 39,020 members eligible to be called by the IVR system. Of those, 27,447 were not reached. Of the 11,573 members who were reached, 11,280 declined to be transferred at the end of the call. Only 293 of the members were transferred to a depression management consultant at the end of the automated call.

Member Characteristics

Member characteristics overall and in each of the 3 IVR call status groups are shown in **Table 1**. The average age of all eligible members was 49.8 years, and they were more likely to be female, located in the Western Pennsylvania region, and live in a rural area. IVR calls were placed evenly over the duration of the study, resulting in 4 evenly distributed 3-month calling periods: December to February, March to May, June to August, and September to November. The 3 most frequently prescribed drugs are escitalopram, setraline, and citalopram, taken by 20.2%, 16.7%, and 15.0% of the members, respectively.

Although we found statistically significant differences in members' age, sex, region, MSA, month of intervention, and drug across the 3 intervention groups, the small *P* values (*P* <.001) were driven by the very large numbers of members in the not reached and reached/not transferred groups. In effect, aside from members' age, the member distributions differed little by sex, region, MSA, and drug. For month of intervention, there are fewer reached/transferred members in September to November and more in December to February compared with the not reached and reached/not transferred groups.

Age is clearly the member characteristic distributed most unevenly across the 3 groups. Of the members who were not reached, 31.3% were 55 years or older, compared with 51.7% and 59.7% in the reached/not transferred and reached/transferred groups, respectively. Even more striking, the 65+ age category represents 41.3% of those who

■ Table 1. Member Characteristics by IVR Call Status

Characteristic	Total (N = 39,020)		Not Reached (N = 27,447)		Reached/ Not Transferred (N = 11,280)		Reached/ Transferred (N = 293)		P Value[a]
Age, y, mean (SD)	49.8	(17.7)	47.5	(17.2)	55.2	(17.9)	58.7	(16.4)	<.001
Age category, No. (%)									
18-24 y	3003	(7.7)	2437	(8.9)	560	(5.0)	6	(2.0)	<.001
25-34 y	5548	(14.2)	4414	(16.1)	1113	(9.9)	21	(7.2)	
35-44 y	7287	(18.7)	5623	(20.5)	1629	(14.4)	35	(11.9)	
45-54 y	8588	(22.0)	6386	(23.3)	2146	(19.0)	56	(19.1)	
55-64 y	6333	(16.2)	4250	(15.5)	2029	(18.0)	54	(18.4)	
≥65 y	8261	(21.2)	4337	(15.8)	3803	(33.7)	121	(41.3)	
Sex, No. (%)									
Male	12,905	(33.1)	9534	(34.7)	3297	(29.2)	74	(25.3)	<.001
Female	26,115	(66.9)	17,913	(65.3)	7983	(70.8)	219	(74.7)	
Region, No. (%)									
Central	7785	(20.0)	5518	(20.1)	2214	(19.6)	53	(18.1)	<.001
Western	30,810	(79.0)	21,676	(79.0)	8898	(78.9)	236	(80.5)	
Other	425	(1.1)	253	(0.9)	168	(1.5)	4	(1.4)	
MSA, No. (%)									
Urban	5817	(14.9)	4126	(15.0)	1622	(14.4)	69	(23.5)	<.001
Rural	25,632	(65.7)	18,042	(65.7)	7420	(65.8)	170	(58.0)	
Suburban	7571	(19.4)	5279	(19.2)	2238	(19.8)	54	(18.4)	
Month of intervention, No. (%)									
December-February	10,198	(26.1)	7029	(25.6)	3069	(27.2)	100	(34.1)	<.001
March-May	10,245	(26.3)	7265	(26.5)	2903	(25.7)	77	(26.3)	
June-August	9070	(23.2)	6460	(23.5)	2547	(22.6)	63	(21.5)	
September-November	9507	(24.4)	6693	(24.4)	2761	(24.5)	53	(18.1)	
Drug, No. (%)									
Escitalopram	7883	(20.2)	5579	(20.3)	2238	(19.8)	66	(22.5)	<.001
Setraline	6512	(16.7)	4483	(16.3)	1972	(17.5)	57	(19.5)	
Citalopram	5863	(15.0)	4036	(14.7)	1784	(15.8)	43	(14.7)	
Fluoxetine	3685	(9.4)	2665	(9.7)	994	(8.8)	26	(8.9)	
Bupropion	3467	(8.9)	2664	(9.7)	791	(7.0)	12	(4.1)	
Venlafaxine hydrochloride XR	2960	(7.6)	2120	(7.7)	817	(7.2)	23	(7.8)	
Paroxetine	2356	(6.0)	1615	(5.9)	724	(6.4)	17	(5.8)	
Other	6294	(16.1)	4285	(15.6)	1960	(17.4)	49	(16.7)	

IVR indicates interactive voice response; XR, extended release.
[a]Test across the 3 IVR call groups. Chi-square test for categorical variables, Kruskal-Wallis for continuous age.

were reached/transferred, but only 15.8% of those who were not reached.

Adherence Rates

The overall acute adherence rate was 57.4%, dropping to 45.6% in the continuation phase (Table 2). We observed this same pattern in each of the 3 intervention groups. For those not reached, the acute and continuation adherence rates were 56.2% and 44.1%, respectively. In the reached/not transferred group, the acute adherence rate was 60.1% and the continuation adherence rate was 49.0%. In those who were reached/transferred, the acute and continuation rates were 63.5% and

■ **Table 2.** Adherence Rates by Member Characteristic and IVR Call Status

Characteristic	Not Reached		Reached/Not Transferred		Reached/Transferred		Total	
	Acute[a]	Continuation[b]	Acute	Continuation	Acute	Continuation	Acute	Continuation
Age category								
18-24 y	33.1	21.1	35.7	25.0	33.3	0.0	33.6	21.8
25-34 y	55.4	39.1	56.5	41.6	47.6	19.1	55.6	39.5
35-44 y	54.0	42.4	50.4	39.9	57.2	48.6	53.2	41.9
45-54 y	54.7	44.6	52.9	44.3	51.8	46.4	54.2	44.6
55-64 y	58.9	49.0	58.7	49.7	64.8	55.6	58.9	49.3
≥65 y	72.4	58.9	73.6	60.9	74.4	60.3	73.0	59.8
Sex								
Male	57.2	43.8	60.6	48.4	68.9	56.8	58.2	45.1
Female	55.6	44.3	59.8	49.2	61.6	49.3	57.0	45.8
Region								
Central	55.5	43.0	58.5	48.2	64.2	50.9	56.4	44.5
Western	56.2	44.4	60.3	49.1	63.1	51.3	57.5	45.8
Other	64.8	46.6	68.5	56.0	75.0	50.0	66.4	50.4
MSA								
Urban	56.6	44.8	63.0	51.7	59.4	46.4	58.4	46.8
Rural	55.8	43.5	59.7	48.6	64.7	52.4	57.0	45.0
Suburban	57.2	45.7	59.2	48.4	64.8	53.7	57.9	46.6
Month of intervention								
December-February	54.5	41.7	58.5	46.1	56.0	44.0	55.7	43.0
March-May	54.3	41.3	58.5	46.9	67.5	52.0	55.6	42.9
June-August	56.2	43.7	59.4	48.0	69.8	55.6	57.1	45.0
September-November	60.1	50.2	64.0	55.4	64.2	58.5	61.3	51.8
Drug								
Escitalopram	58.6	46.1	63.9	51.2	57.6	42.4	60.1	47.6
Setraline	59.4	48.1	63.3	54.5	68.4	50.9	60.7	50.1
Citalopram	56.0	43.0	59.7	47.3	55.8	41.9	57.1	44.3
Fluoxetine	55.2	42.6	59.0	47.1	58.0	50.0	56.2	43.9
Bupropion	50.2	37.1	56.4	45.1	75.0	66.7	51.7	39.0
Venlafaxine hydrochloride XR	59.1	48.5	58.1	49.0	73.9	65.2	58.9	48.8
Paroxetine	59.1	48.3	63.1	53.2	58.8	58.8	60.4	49.9
Other	51.6	40.0	54.5	43.5	69.4	59.2	52.7	41.3
Total	56.2	44.1	60.1	49.0	63.5	51.2	57.4	45.6

IVR indicates interactive voice response.
[a] 3 months
[b] 6 months

51.2%, respectively. Although the rates drop at the continuation phase across all 3 intervention groups, the adherence rates increase with an increasing level of involvement in the intervention.

The overall acute and continuation adherence rates increase with increasing age. At 3 months, the rate increased from 33.6% in the 18 to 24 year olds to 73% in the members who were 65 years or older. We observed almost identical patterns within each of the 3 intervention groups, where 33% to 35% of the 18 to 24 year olds were adherent at the acute stage while over 72% of the members 65 years or older were adherent. Adherence rates were similar within the sex and MSA subgroups. The adherence rates were highest in the other region compared with both the Central Pennsylvania and West-

■ Table 3. GEE Model Results—Univariate Associations

Characteristic	Compliance		
	OR[a]	95% CI	*P* Value
Intervention group		global *P* value	<.001
Not reached	1.00	—	
Reached/not transferred	1.20	(1.15-1.25)	<.001
Reached/transferred	1.34	(1.07-1.67)	.010
Time			
Acute	1.00	—	
Continuation	0.62	(0.61-0.63)	<.001
Age group		global *P* value	<.001
18-24 y	1.00	—	
25-34 y	2.36	(2.15-2.58)	<.001
35-44 y	2.35	(2.15-2.56)	<.001
45-54 y	2.53	(2.32-2.75)	<.001
55-64 y	3.07	(2.81-3.36)	<.001
≥65 y	5.11	(4.69-5.57)	<.001
Sex			
Male	1.00	—	
Female	0.99	(0.95-1.03)	.697
Region		global *P* value	.002
Central	1.00	—	
Western	1.05	(1.00-1.10)	.050
Other	1.36	(1.13-1.64)	.001
MSA		global *P* value	.020
Urban	1.00	—	
Rural	0.94	(0.89-0.99)	.020
Suburban	0.99	(0.92-1.05)	.647
Month of intervention		global *P* value	<.001
December-February	1.00	—	
March-May	1.00	(0.95-1.05)	.874
June-August	1.07	(1.01-1.13)	.013
September-November	1.35	(1.27-1.42)	<.001
Drug		global *P* value	<.001
Other	1.00	—	
Escitalopram	1.32	(1.24-1.41)	<.001
Setraline	1.41	(1.32-1.51)	<.001
Citalopram	1.17	(1.09-1.25)	<.001
Fluoxetine	1.13	(1.05-1.23)	.001
Bupropion	0.94	(0.87-1.02)	.122
Venlafaxine hydrochloride XR	1.33	(1.22-1.44)	<.001
Paroxetine	1.40	(1.28-1.53)	<.001

CI indicates confidence interval; GEE, generalized estimating equation; XR, extended release.
[a]"Univariate" models were also adjusted for time.

ern Pennsylvania regions. We also observed some differences in the drug and month of intervention groups, differences that show the same pattern at both the acute and continuation phase. Members who were called in September, October, and November had higher adherence rates compared with the other 3-month categories.

Univariate Models

We ran GEE models for each of the member characteristics individually (**Table 3**). Because of the longitudinal nature of the outcomes, time was included as a covariate for each of the other characteristics even though we reported these as univariate associations. Compared with the baseline, not reached group, adherence is significantly higher in the reached/not transferred and reached/transferred groups (odds ratio [OR] = 1.20 and 1.34, respectively). The model with time as the only covariate shows the significant decrease in adherence observed at the continuation phase compared with the acute phase (OR = 0.62, *P* value <.001). The univariate associations mirror the adherence rate patterns observed in Table 2, as they should. Except for sex, which is not a significant predictor of adherence, all global *P* values and most of the category-specific odds ratios are statistically significant at the 0.05 level.

Adherence increased markedly with age group, with members older than

■ **Table 4.** GEE Model Results—Multivariate Analysis

Characteristic	Adjusted[a] OR	95% CI	P Value	Adjusted[b] OR	95% CI	P	Adjusted[c] OR	95% CI	P Value
Intervention Group		global P value	<.001		global P value	<.001		global P value	.956
Not reached	1.00	—		1.00	—		1.00	—	
Reached/not transferred	1.20	(1.15-1.25)	<.001	1.19	(1.14-1.24)	<.001	1.00	(0.96-1.04)	.993
Reached/transferred	1.34	(1.07-1.67)	.010	1.34	(1.08-1.68)	.009	1.03	(0.83-1.30)	.766

CI indicates confidence interval; GEE, generalized estimating equation; OR, odds ratio.
[a]Adjusted for time.
[b]Adjusted for time, month of intervention, and drug.
[c]Adjusted for time, age group, month of intervention, and drug.

65 years having a 5.11 higher odds of adherence than the baseline group aged 18 to 24 years. The lower adherence in members prescribed bupropion compared with "other" drugs is once again observed; however, the odds ratio of 0.94 is not statistically significant (P value = .122).

Adjusted Models

Table 4 shows multivariable GEE adherence ORs for the 3 intervention groups. Region, MSA, and sex were not significant predictors in the adjusted models and were not included as covariates. The first column of the table shows the intervention group ORs adjusted for time only. The second column is the model adjusted for time, month of intervention, and drug. The OR for the reached/transferred and reached/not transferred groups compared with the not reached baseline are 1.34 and 1.19, respectively (P values .009 and <.001). These ORs are nearly identical to the model adjusted for time only, suggesting better adherence in those members who listened to the call and were transferred to a depression management consultant and those who listened to the call and declined transfer.

The final model shown in the third column of Table 4 was adjusted for the categorical age variable as well as time, month of intervention, and drug. The ORs for adherence in the reached/not transferred and reached/transferred intervention groups are now 1.00 and 1.03, respectively (P values = .993 and .766), indicating no difference in adherence in the 3 member groups.

DISCUSSION

Crude Adherence Rates

If the crude adherence rates in the 3 intervention groups are compared at the acute time period, members who were reached/transferred appear to have better adherence than members who were reached/not transferred or those who were not reached (63.5% vs 60.1% and 56.2%, respectively). The same pattern is observed at the continuation phase; however, the rates are lower in each group. If only the crude rates were analyzed, one might conclude that the IVR phone calls alone (reached/not transferred) or in conjunction with a transfer to a depression case manager (reached/transferred) increase adherence compared with those who did not listen to the phone call (not reached).

Adherence by Age

Examination of the adherence rates by age show an increase in adherence from the 18 to 24 year age group to the 25 to 34 year olds, where the rates are relatively stable or increase slightly through the 55 to 64 year olds. The adherence rates then jump to the highest levels in the members who are 65 years or older (Table 2).

Reaching Members by Age

The 3 intervention groups are defined based on a member's willingness to listen to an IVR call and to transfer to a depression management consultant, which may be related to some member characteristic. If this study were a randomized controlled trial, these characteristics, such as age, would be balanced across treatment groups; however, inclusion in 1 of the 3 intervention groups in our study was not random. Table 1 summarizes the distribution of the member characteristics overall and in the 3 phone call status groups and shows that the member characteristics are relatively evenly distributed for most factors except age. Of the members who were reached/transferred, 41.3% are 65 years or older compared with only 15.8% of the members who were not reached. Of the 8261 members 65 years or older in the study, 1.5% (121/8261) were reached/transferred, compared with only 0.2% of the 18 to 24 year olds (6/3003). It appears that the oldest members are more willing to listen to the entire IVR call and more likely to request transfer to a depression manager than the youngest members. It is possible that older members are no longer working and are at home when the call is placed. They may also have more questions or concerns about their depression and may wish to speak to a consultant. Younger members may feel they do not need any help with the management of their depression or may not be as willing to spend the time on the call as older members.

■ **Figure 2**. Member Adherence by Age and IVR Phone Call Status
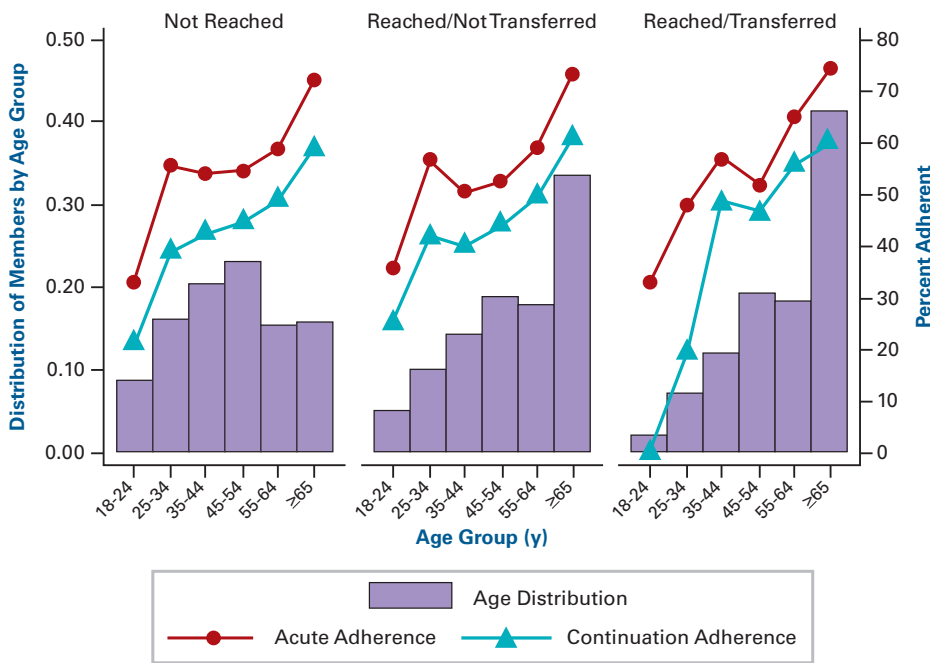
IVR indicates interactive voice response.

■ **Figure 3**. Age as a Confounder
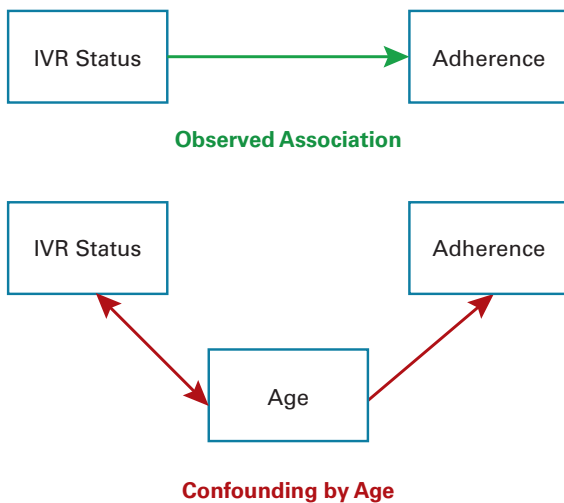
IVR indicates interactive voice response.

Confounding by Age

Whatever the reason for the difference in age in members who were reached and not reached, age was related to both adherence rates and the IVR call status defining the 3 comparison groups. This relationship is displayed in **Figure 2**. The connected lines show the increase in acute and continuation adherence with increasing age. The bars show the distribution of member ages in each of the 3 call status groups. The adherence rates are similar across groups; however, the age distributions are not. The reached/ not transferred and reached/ transferred groups have over 30% and 40%, respectively, of the members in the upper age category compared with 15% in the not reached group.

Thus, our analysis of adherence rates without factor adjustment is clearly confounded positively (ie, results biased away from the null) by age. Had we not statistically adjusted for confounding by age group, we would have falsely concluded that IVR calls were highly effective overall as a method for improving antidepressant medication adherence across all members, when in fact IVR calls had little or no impact on adherence rates. These relationships are depicted graphically in **Figure 3**.

In addition to identifying age group as an important confounding variable when evaluating the association between IVR calls and antidepressant medication adherence, we found in our age-adjusted analysis that IVR calls had little or no impact on adherence rates. That is, we observed similar, marked increases in adherence rates with increasing age in each of the 3 intervention groups examined. This observation suggests that other intervention strategies to improve antidepressant medication adherence should focus on the younger segment of the patient population.

The results of our evaluation, in which patients were self-selected into 1 of 3 intervention groups, are consistent with those of Stuart et al,[19] who conducted a randomized controlled clinical trial of antidepressant medication compliance based on 647 patients from 30 primary care study sites. In this trial, all patients at a given site were randomly assigned to 1 of 3 intervention strategies: (1) education, (2) education and call, and (3) education, call, and IVR. Medication compliance was measured at 2 weeks, and 2, 4, 6, 9, and 12 months. The authors found no statistically significant differences in patient compliance among the 3 intervention strategies, indicating that the addition of the IVR system did not prove to be either more or less effective than the other 2 conventional strategies.

As a result of the current evaluation, Highmark temporarily stopped the antidepressant IVR calls, and initiated outreach through its behavioral health department. The Highmark behavioral health case managers began calling these members as of April 2011. Highmark will continue to monitor the Antidepressant Medication Management HEDIS results annually, and determine the most suitable outreach modality to assist members based on their individual life stage.

CONCLUSIONS

Evaluations of the effectiveness of intervention programs must carefully account for potential confounding by 1 or more study factors including age group, which may be related to both intervention group and intervention outcome. Our evaluation of the effectiveness of IVR calls as an intervention strategy for improving antidepressant medication adherence was confounded positively by age group. This result helped us to identify that IVR calls had little or no impact on adherence rates and that adherence rates generally increased markedly with increasing age, a key finding that may help target other intervention strategies. Although IVR is widely used throughout the country, it is crucial that health plans assess the unique needs of their membership.[15] These results were the impetus for Highmark exploring the best alternative outreach strategies for assisting younger members. Highmark continues to explore utilizing all the various technology to target its member outreach based on the different life stages of its members.

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