1-10-2018

Evaluating Factors Impacting Medication Adherence Among Rural, Urban, and Suburban Populations

Cody Arbuckle
Chapman University, arbuc100@mail.chapman.edu

Daniel M. Tomaszewski
Chapman University, tomaszew@chapman.edu

Benjamin D. Aronson
Ohio Northern University

Lawrence M. Brown
Chapman University, lbbrown@chapman.edu

Jon C. Schommer
University of Minnesota

See next page for additional authors

Follow this and additional works at: https://digitalcommons.chapman.edu/pharmacy_articles

Recommended Citation

Evaluating Factors Impacting Medication Adherence Among Rural, Urban, and Suburban Populations

Authors

Cody Arbuckle, Daniel M. Tomaszewski, Benjamin D. Aronson, Lawrence M. Brown, Jon C. Schommer, Donald Morisky, and Erik J. Linstead

Evaluating Factors Impacting Medication Adherence Among Rural, Urban, and Suburban Populations

Cody Arbuckle, MS;[1] Daniel Tomaszewski, PharmD, PhD;[2] Benjamin D. Aronson, PharmD, PhD;[3] Lawrence Brown, PharmD, PhD;[2] Jon Schommer, PhD;[4] Donald Morisky, ScD;[5] & Erik Linstead, PhD[1]

1 Mathematics and Computer Science, Schmid College of Science and Technology, Chapman University, Orange, California
2 Department of Biomedical and Pharmaceutical Sciences, School of Pharmacy, Chapman University, Irvine, California
3 Department of Pharmacy Practice, College of Pharmacy, Ohio Northern University, Ada, Ohio
4 Department of Pharmaceutical Care and Health Systems, College of Pharmacy, University of Minnesota, Minneapolis, Minnesota
5 Department of Community Health Sciences, Fielding School of Public Health, University of California, Los Angeles, California

Abstract

Purpose: To evaluate differences in prescription medication adherence rates, as well as influencing factors, in rural and urban adults.

Methods: This is a retrospective analysis of the 2015 National Consumer Survey on the Medication Experience and Pharmacists' Role. A total of 26,173 participants completed the survey and provided usable data. Participants using between 1 and 30 prescription medications and living more than 0 miles and up to 200 miles from their nearest pharmacy were selected for the study, resulting in a total of 15,933 participants. Data from the 2010 US Census and Rural Health Research Center were used to determine the population density of each participant's ZIP code. Participant adherence to reported chronic medications was measured based on the 8-item Morisky Medication Adherence Scale (MMAS-8).

Findings: Overall adherence rates did not differ significantly between rural and urban adults with average adherence based on MMAS-8 scores of 5.58 and 5.64, respectively ($P = .253$). Age, income, education, male sex, and white race/ethnicity were associated with higher adherence rates. While the overall adherence rates between urban and rural adults were not significantly different, the factors that influenced adherence varied between age-specific population density groupings.

Conclusion: These analyses suggest that there is no significant difference in adherence between rural and urban populations; however, the factors contributing to medication adherence may vary based on age and population density. Future adherence intervention methods should be designed with consideration for these individualized factors.

Key words access to care, health care access, medication adherence, medication use, pharmacy.

Medication nonadherence is considered one of the greatest modifiable health risks to exist in the United States. Nearly half of all Americans who are prescribed a prescription medication are nonadherent to it.[1] The presence of nonadherence to prescription medications causes poor health-related outcomes. Nonadherence has been shown to increase the likelihood of disease progression, lead to higher utilization of health care services, increase the cost of care, and cause higher mortality rates.[2-9]

The cause of nonadherence is complex and there are many factors that have been linked to increasing rates of nonadherence. These include factors related to the cost of the medications, socioeconomic status, and convenience.[10-15] With increasing rates of poverty

among those living in rural areas, overall lower median household income for rural dwellers compared to urban dwellers, reduced rates of insurance coverage for rural dwellers, and increased distance to health care services among individuals living in rural communities, one would assume the risk of nonadherence is increased among those living in rural communities.[16-19]

Nearly 50 million individuals are reported to live in rural settings across the United States.[19] Research has continued to show that health-related outcomes are often worse across chronic diseases for individuals living in rural settings.[17,20] The cause of these poor outcomes is often the center of debate; however, some studies have suggested that access to health care services and medications may contribute.[17,21,22] There has been limited research to assess differences in medication adherence in rural and urban communities.[23] As most chronic conditions are currently treated through the use of chronic prescription medications, it is important to evaluate if differences in the use of prescription medications exist between rural and urban populations.

The objective of this study is to compare adherence rates between rural and urban populations. Additionally, the study evaluates differences between known factors that impact adherence among rural and urban populations.

Methods

Database

This study was a retrospective analysis of the 2015 National Consumer Survey on the Medication Experience and Pharmacists' Role. The 2015 National Consumer Survey was conducted using Qualtrics Panels (Qualtrics LLC, Provo, Utah) to provide participant panels and enroll participants based on census statistics for geographic location, age, and gender. Qualtrics Panels is an online sample of study participants maintained by the online survey system, Qualtrics. Participants were recruited online actively by Qualtrics from this sample and results were provided to researchers. All communications to potential participants were delivered electronically. Participation stratification was included to ensure a minimum of 500 respondents from each of the 50 states and the District of Columbia. A total of 26,173 participants completed the study and provided useable data.

Study Population

The study sample included US residents aged 18 years and older at the time of completion. The data were collected in 2015. The sample included all participants from the original data set, but it was limited to those using prescription medications. Data were restricted to include those using between 1 and 30 prescription medications. Additionally, participants with incomplete responses and those reporting living over 200 miles from the nearest pharmacy or living 0 miles from the nearest pharmacy were excluded from the sample.

Variables

Adherence to reported chronic medications was measured based on the 8-item Morisky Medication Adherence Scale (MMAS-8). The scale has been proven to be a reliable and valid measure of patient-reported adherence.[24-26] The scoring of responses range from 0 (worse possible adherence score) to 8 (best possible adherence score). The scores for participant MMAS-8 were reported both as raw scores ranging from 0 to 8 and grouped by level of adherence, with those scoring less than 6 being defined as low adherers, those scoring 6 to less than 8 defined as medium adherers, and those scoring 8 as high adherers, as recommended.[24]

Participant-reported ZIP codes were compared to rural-urban commuting area (RUCA) scores compiled by the Rural Health Research Center to assign each participant's population density as rural, suburban, or urban. RUCA scores classify US Census tracts using measures of population density, urbanization, and daily commuting. The latest version of RUCA scoring, based on 2010 Census data, provides a cross-walk between ZIP codes and RUCA score. Participants residing in a ZIP code with a RUCA score of greater than 6 were defined as rural, those with a RUCA score of between 2 and 6 were defined as suburban, and those with a RUCA score of 1 were defined as urban.

An abbreviated version of the Beliefs about Medicines Questionnaire (BMQ) was used to gain participants' perception regarding the necessity of and concerns about medications.[27] Individual question responses were used to establish participant harm, overuse, life-saving, and burden belief. Composite scoring for the BMQ was not used as the survey did not include the full BMQ questionnaire, which restricted scoring to responses to individual items. Participants rated agreement with included statements based on a 7-point Likert scale. Based upon the Concerns-Necessity Framework, necessity beliefs have previously been shown to be positively related to medication adherence, while concerns, overuse beliefs, and harm beliefs have been shown to be negatively related.[28] Additionally, respondents were also asked to rate their level of agreement using the same Likert scale to the statement, "Purchasing medications causes me financial hardship." This served as the marker for financial

hardship, with higher numerical values being associated with greater levels of agreement that purchasing medications cause financial hardship. Participants were also asked to rate their overall health on a 4-point scale, ranging from excellent to poor.

Analysis

Participant demographics and characteristics, medication adherence, and population density of ZIP code were reported using descriptive statistics. Multivariate regression analyses were used to assess associations between medication adherence (the dependent variable) and education level, household income, medications causing financial hardship, age, self-rated health score, distance to the nearest pharmacy, use of mail order pharmacies, use of the drive-through at their pharmacy, medication burden belief, medication life-saving belief, medication overuse belief, total number of prescription medications taken daily, and medication harm belief (independent variables). All independent variables were added to the models at the same time. Education level, household income, use of mail order pharmacies, and use of a drive-through at the pharmacy were treated as categorical variables, with lowest level of education and lowest income level serving as the reference level. As it was hypothesized that the importance of these factors differed between rural, suburban, and urban participants, separate models were constructed for each cohort. Additionally, these cohorts were further deconstructed by age groups because of the significant difference in age groupings between cohorts, and regression models were constructed for each subset.

Software

All participants' records were stored in a relational database using the open-source database software MySQL (v. 5.7.11, Oracle, Redwood Shores, California). All analytics were performed using the open-source statistical computing software R (v 3.2.3, R Foundation, Vienna, Austria).

Results

Of the 26,173 participants, 16,677 reported taking between 1 and 30 prescription medications. Of those taking prescription medications, a total of 15,933 participants met the additional inclusion criteria. Based on the 2010 RUCA designations, a total of 1,735 participants were rural dwellers, 5,302 were suburban dwellers, and 8,896 urban dwellers.

The demographic makeup of the 3 levels of population density varied significantly, with individuals under the age of 41 making up over 44% of the population for urban centers while this same age group accounted for only 35% of the population in rural areas. Conversely, individuals over the age of 54 accounted for a larger proportion of rural participants, with 44% of them living in rural areas and 37% in urban areas. The difference in the age distribution results in rural areas having an average age of 49.1 years and urban areas having an average age of 46.3 years ($P < .005$; Table 1).

Income distribution was similarly unevenly distributed between the 3 subgroups. The percentage of individuals with a household income of less than $40,000 per year was greatest among rural participants, compared to suburban and urban areas (54.9%, 46.2%, and 39.7%, respectively). Differences also existed by educational status, sex, and ethnicity. Table 1 provides further demographic information about the participants contained within each group. The overall mean adherence score based on the MMAS-8 was 5.6 (SD = 2.0) for all participants. The mean adherence score was compared for rural, suburban, and urban participants, as was the proportion of participants meeting certain adherence criteria. There was no significant difference between each of the groups based on mean adherence scores (Table 2). Rurality groups had roughly equivalent proportions of individuals classified as low adherence (MMAS-8 < 6; rural 49.5%, suburban 50.3%, and urban 50.7%), medium adherence (MMAS-8 ≥ 6 and < 8; rural 27.5%, suburban 28.2%, and urban 28.3%) and high adherence (MMAS-8 = 8; rural 23.1%, suburban 21.6%, and urban 21.0%; Table 2).

Based on subset analyses of each of the designations according to population density, similar adherence scores were also shown between rural, suburban, and urban participants when categorized by other demographic factors. For instance, there were no statistically significant differences in medication adherence scores between rural, urban, and suburban participants when comparing the same age groups, income groups, education level, sex, and ethnicity (Table 3).

A multivariable linear regression was constructed for all participants, as well as separately for rural participants and urban participants (Table 4). The results of the overall and separated rural versus urban regression models showed similarities. However, some factors included in the model had significance only in urban participants and not rural participants, including distance to pharmacy (B = −0.01, $P < .001$), use of mail order pharmacies (B = −0.14, $P = .002$), and perceptions of medication-related factors.

To better understand potential differences among various age groups of rural and urban dwellers, a series of

Table 1 Demographics of Participants, Separated Based on Rural, Suburban, or Urban Dwelling

Variables	Rural	Suburban	Urban	Significance[a]
Total participants	1,735 (10.9%)	5,302 (33.28%)	8,896 (55.83%)	
Mean age	49.1	47.9	46.3	<.005
Mean medication count	3.7	3.6	3.3	<.005
Age group				
18-29	245 (14.1%)	872 (16.5%)	1,832 (20.6%)	<.005
30-41	357 (20.6%)	1,131 (21.3%)	2,112 (23.7%)	<.005
42-53	376 (21.7%)	1,155 (21.8%)	1,642 (18.5%)	<.005
54-65	406 (23.4%)	1,118 (21.1%)	1,590 (17.9%)	<.005
Over 65	351 (20.2%)	1,026 (19.4%)	1,720 (19.3%)	.676
Income				
Income at or below $40,000	953 (54.9%)	2,451 (46.2%)	3,528 (39.7%)	<.005
Income between $41,000 and $100,000	658 (37.9%)	2,360 (44.5%)	4,193 (47.1%)	<.005
Income over $100,000	124 (7.2%)	491 (9.3%)	1,175 (13.2%)	<.005
Education				
High school degree or less	521 (30.0%)	1,283 (24.2%)	1,673 (18.8%)	<.005
Some college to bachelor's degree	1,052 (60.6%)	3,463 (65.3%)	5,961 (67.0%)	<.005
Advanced degree	162 (9.3%)	556 (10.5%)	1,262 (14.2%)	<.005
Sex				
Male	409 (23.6%)	1,374 (25.9%)	2,585 (29.1%)	<.005
Female	1,326 (76.4%)	3,928 (74.1%)	6,311 (70.9%)	<.005
Ethnicity				
White	1,594 (91.9%)	4,681 (88.3%)	7,101 (79.8%)	<.005
Non white	141 (8.1%)	621 (11.7%)	1,795 (20.2%)	<.005

[a]Significance reported as *P* values from chi-square difference test.
P < .05 considered significant.

Table 2 Adherence Rates within Rural, Urban, and Suburban Settings

	Rural (N = 1,735)	Suburban (N = 5,302)	Urban (N = 8,896)	Significance
Average MMAS-8 score (SD)[a]	5.64 (2.04)	5.64 (2.02)	5.58 (2.05)	.253
Low adherence N (%)[b]	858 (49.5%)	2,664 (50.3%)	4,511 (50.7%)	.604
Medium adherence N (%)[b]	477 (27.5%)	1,493 (28.2%)	2,514 (28.3%)	.809
High adherence N (%)[b]	400 (23.1%)	1,145 (21.6%)	1,871 (21.0%)	.162

[a]Significance reported as *P* values from Kruskall–Wallis comparing differences between groups.
[b]Significance reported as *P* values from chi-square difference test.
Use of the MMAS-8 is protected by US copyright laws. Permission for use is required. A license agreement is available from Donald E. Morisky, 294 Lindura Court, Las Vegas, NV 8,9138-4,632; dmorisky@gmail.com.

multivariable linear regression subset analyses were conducted. The results for rural versus urban cohorts based on age groupings (aged 18-41, 42-64, and 65+) can be found in Table 5. According to the regression analysis, factors that are significantly associated with adherence varied dependent on population density and age groupings. Comparing urban and rural while holding age group constant revealed differences and similarities between rural and urban participants. For instance, adherence of rural and urban participants aged 65 and older were both impacted by financial hardship (*P* = .004, *P* < .001, respectively) and perception of medication as a burden (*P* = .010, *P* < .001, respectively); whereas only the adherence for urban individuals over 65 years of age was impacted

by the use of drive-through pharmacies (*P* < .001), and their overall health ranking (*P* < .001).

Discussion

Among all the different demographic factors, age had the largest impact on adherence with those aged 18-29 reporting an average mean score of 4.85, while those aged 65 and over reported an average adherence score of 6.69, with a higher score equating to better adherence. Additionally, increased income, increased education level, male sex, and white race/ethnicity are all associated with increased adherence for all participants in this study.

Table 3 Adherence Scores among Different Demographic Groups Based on Rural, Suburban, or Urban Dwelling

Variables Age Group	Rural Mean MMAS-8 Score (SD)	Suburban Mean MMAS-8 Score (SD)	Urban Mean MMAS-8 Score (SD)	Overall Mean MMAS-8 Score (SD)
18-29	4.86 (2.07)	4.82 (2.12)	4.85 (2.07)	4.85 (2.09)
30-41	4.98 (2.21)	5.06 (2.09)	5.02 (2.12)	5.03 (2.12)
42-53	5.53 (1.99)	5.48 (1.98)	5.50 (2.04)	5.50 (2.01)
54-65	5.97 (1.87)	6.04 (1.78)	6.04 (1.81)	6.03 (1.81)
Over 65	6.59 (1.54)	6.70 (1.50)	6.70 (1.50)	6.69 (1.50)
Income				
Income at or below $40,000	5.47 (2.10)	5.46 (2.07)	5.43 (2.08)	5.45 (2.08)
Income between $41,000 and $100,000	5.86 (1.96)	5.75 (1.98)	5.61 (2.04)	5.68 (2.02)
Income over $100,000	5.79 (1.88)	6.01 (1.85)	5.94 (1.92)	5.95 (1.90)
Education				
High school degree or less	5.65 (2.05)	5.62 (2.05)	5.59 (2.05)	5.61 (2.05)
Some college to bachelor's degree	5.61 (2.04)	5.61 (2.00)	5.54 (2.04)	5.57 (2.03)
Advanced degree	5.84 (1.99)	5.87 (2.00)	5.79 (2.08)	5.82 (2.05)
Sex				
Male	5.85 (1.93)	5.90 (1.94)	5.69 (2.06)	5.77 (2.02)
Female	5.58 (2.07)	5.54 (2.04)	5.54 (2.04)	5.55 (2.04)
Ethnicity				
White	5.71 (2.01)	5.72 (1.99)	5.72 (2.01)	5.72 (2.00)
Other	4.86 (2.23)	5.03 (2.14)	5.06 (2.13)	5.04 (2.14)

Initial interpretation of the data suggests that medication use and adherence is the same between rural, suburban, and urban individuals. This is, however, complicated by the fact that participant demographics and general characteristics are different between each of these groups. Previous research has established positive relationships with age and female sex with increased adherence to prescription medications. With the rural group of participants being significantly older and having a larger proportion of females than suburban and urban participants, one would assume that the rural group would have increased adherence rates.[29,30] This is, however, counterbalanced by the fact the rural participants reported lower income levels and an increased distance to the nearest pharmacy, which are associated with lower levels of medication adherence.

Based on separate regression analyses for rural and urban participants, the demographic and belief factors impacting adherence between rural and urban participants vary (Tables 4 and 5). Adherence for rural participants over the age of 65 was negatively influenced by financial hardship of medications, whereas adherence for these individuals was positively impacted by perceptions of medication burden. Alternatively, adherence for urban participants over the age of 65 was negatively impacted by financial hardship, use of drive-through pharmacies, and overall health ratings, but adherence was positively affected by perceptions of medication burden.

Additionally, differences between factors that impact adherence among different age groups of rural partici-

pants were shown. For instance, adherence for individuals aged 18-41 and 42-65 was impacted by overall health score and use of drive-through pharmacies, while these 2 variables were not related to adherence of rural participants older than 65. The differential relationship between self-rated health status and adherence based on age of rural participants may suggest that younger rural participants with worse perceived health place increased importance on adhering to their medication.

Financial hardship was shown to negatively impact adherence across all age groups, regardless of being identified as urban or rural dwellers. Although this factor impacts medication for participants from all population densities, it was hypothesized that this would be of greater importance for rural participants, considering the higher levels of poverty and lower median household incomes reported in rural areas compared to urban areas.[31] This was, however, not supported by the results of this study, which suggested financial hardship was equally impactful for urban and rural dwellers. It is important to note that the negative correlation between financial hardship and adherence should be interpreted as higher levels of agreement that medications cause financial hardship is associated with lower MMAS-8 scores, which equates to worse adherence. Similarly, the use of a drive-through at the pharmacy was associated with worse adherence, hence, the negative beta coefficient reported in Table 4. However, this study is not able to determine if these relationships are causative in nature. Additional research is needed to evaluate this further.

Table 4 Linear Regression of MMAS-8 Scores in Total Participant Population and Separated by Urban and Rural Population Densities

	All Participants		All Rural Participants		All Urban Participants	
	B*	P	B*	P	B*	P
(Intercept)	4.17	<.001	4.17	<.001	4.27	<.001
Education level[a]	−0.07	0.004	−0.09	0.269	−0.05	0.128
Household income[a]	0.06	0.011	0.06	0.457	0.06	0.052
Financial hardship[b]	−0.16	<.001	−0.16	<.001	−0.16	<.001
Age	0.04	<.001	0.04	<.001	0.04	<.001
Overall health	−0.43	<.001	−0.41	<.001	−0.45	<.001
Distance	0.00	0.106	0.00	0.062	−0.01	<.001
Mail order pharmacy usage[c]	−0.08	0.019	−0.05	0.664	−0.14	0.002
Drive-through usage[c]	−0.30	<.001	−0.35	<.001	−0.32	<.001
Burden	0.18	<.001	0.21	<.001	0.18	<.001
Life-saving	0.04	<.001	0.06	0.026	0.05	<.001
Overprescribed	0.05	<.001	0.07	0.064	0.05	<.001
Harm	0.10	<.001	0.04	0.298	0.09	<.001
Number of prescription medications	−0.02	0.002	−0.04	0.016	−0.02	0.029
Observations	15,933		1,735		8,896	
R^2/adj. R^2	.224/.223		.215/.209		.232/.231	

∗Beta-coefficients reporting negative values indicate a negative association with adherence.

[a]Education level and household income were input using categorical values, with lowest education level and lowest household income category serving as the reference level.

[b]Financial hardship was input as a continuous variable, with higher values relating to increased level of agreement of financial hardship caused by medications.

[c]Factors reported categorically with no serving as the reference level.

Table 5 Subset Multilinear Regression Analysis for Rural and Urban Participants Based on Age Groups

	Rural 18-41		Urban 18-41		Rural 42-65		Urban 42-65		Rural 65+		Urban 65+	
	B	P	B	P	B	P	B	P	B	P	B	P
(Intercept)	5.26	<.001	5.58	<.001	6.43	<.001	5.93	<.001	6.29	<.001	6.53	<.001
Education level	0.04	.787	−0.01	.883	−0.30	.009	−0.10	.090	0.26	.050	0.03	.552
Household income	0.25	.098	0.13	.013	0.01	.950	0.07	.143	−0.20	.161	−0.02	.755
Financial hardship	−0.18	<.001	−0.19	<.001	−0.18	<.001	−0.15	<.001	−0.15	.004	−0.12	<.001
Overall health	−0.61	<.001	−0.52	<.001	−0.36	<.001	−0.43	<.001	−0.15	.272	−0.24	<.001
Distance	0.01	.081	−0.01	.002	0.01	.006	−0.01	.031	−0.01	.074	−0.01	.169
Mail order pharmacy usage	−0.25	.317	−0.45	<.001	−0.08	.622	0.19	.014	0.13	.423	−0.08	.240
Drive−through usage	−0.42	.014	−0.34	<.001	−0.39	.010	−0.30	<.001	−0.24	.276	−0.35	<.001
Burden	0.25	<.001	0.16	<.001	0.22	<.001	0.23	<.001	0.16	.010	0.17	<.001
Life-saving	0.09	.060	0.07	<.001	0.06	.161	0.03	.172	0.07	.245	0.05	.057
Overprescribed	0.08	.190	0.05	.074	0.07	.205	0.05	.056	−0.08	.295	0.06	.051
Harm	−0.03	.646	0.09	<.001	0.05	.375	0.08	.005	0.14	.059	0.04	.216
Number of prescription medications	−0.01	.819	−0.03	.030	−0.05	.037	0.01	.650	−0.06	.057	−0.03	.032
Observations	602		3,944		782		3,232		351		1,720	
R^2/adj. R^2	.151/.134		.147/.144		.152/.139		.134/.130		.139/.109		.138/.132	

Limitations

This study had a number of limitations that the authors wish to describe. First, data collection was conducted electronically, which requires individuals to have internet and computer access to enroll in the study. This may have been a limiting factor for both older populations and those living in more rural areas. Second, the use of a self-reported adherence scale, such as the MMAS-8, does limit the researchers' ability to verify the accuracy of the levels of adherence reported. The MMAS-8 has been widely used and validated, but self-reporting

of adherence without incorporation of additional metrics has potential limitations. Additionally, the data collected only allowed researchers to report correlations between individual factors and adherence. The nature of the data collected does not allow researchers to determine if each factor is causative in nature, which would require additional data collection. Last, it is important to note that each subgroup did not contain the same number of responses.

Conclusion

The percentage of participants falling into the low adherence category, approximately 50%, is similar between rural, urban, and suburban dwellers. This finding is similar to previous research in medication adherence and is generally concerning. When comparing factors impacting adherence between rural and urban individuals and those of different age clusters, distinct overall factors influencing adherence were identified for each group. However, many adherence interventions to date target a single variable identified as a potential factor that impacts adherence. Based on the results of this study, adherence interventions should be further individualized, particularly when considering population density and age.

Development of screening tools and targeted adherence approaches may increase the success of such adherence interventions. One factor that should be evaluated among all participants is the impact of financial hardship on medication use, as all participant groups had negative associations between financial hardship and adherence. Additionally, the use of the drive-through at local pharmacies should be further reviewed, as the reported use of such services was negatively associated with adherence across all participant groups.

References

1. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(5):487-497.
2. Bijlsma MJ, Vansteelandt S, Janssen F, Hak E. The effect of adherence to statin therapy on cardiovascular mortality: quantification of unmeasured bias using falsification end-points. *BMC Public Health*. 2016;16(303):1-8.
3. Horwitz RI, Horwitz SM. Adherence to treatment and health outcomes. *Arch Intern Med*. 1993;153(16):1863-1868.
4. Horwitz RI, Viscoli CM, Berkman L, et al. Treatment adherence and risk of death after a myocardial infarction. *Lancet*. 1990;336(8714):542-545.
5. Krivoy A, Balicer RD, Feldman B, et al. Adherence to antidepressants is associated with lower mortality: a 4-year population-based cohort study. *J Clin Psychiat*. 2016;77(5):e566-e572.
6. McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. *Ann Pharmacother*. 2002;36(9):1331-1336.
7. Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA*. 2007;297(2):177-186.
8. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-530.
9. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004;42(3):200-209.
10. Reach G. Is there an impatience genotype leading to non-adherence to long-term therapies? *Diabetologia*. 2010;53(8):1562-1567.
11. Brunner R, Dunbar-Jacob J, Leboff MS, et al. Predictors of adherence in the women's health initiative calcium and vitamin D trial. *Behav Med*. 2009;34(4):145-155.
12. Molloy GJ, Perkins-Porras L, Strike PC, Steptoe A. Social networks and partner stress as predictors of adherence to medication, rehabilitation attendance, and quality of life following acute coronary syndrome. *Health Psychol*. 2008;27(1):52-58.
13. Kennedy J, Tuleu I, Mackay K. Unfilled prescriptions of Medicare beneficiaries: prevalence, reasons, and types of medicines prescribed. *J Manag Care Pharm*. 2008;14(6):553-560.
14. Chapman RH, Petrilla AA, Benner JS, Schwartz JS, Tang SS. Predictors of adherence to concomitant antihypertensive and lipid-lowering medications in older adults: a retrospective, cohort study. *Drugs Aging*. 2008;25(10):885-892.
15. Jones G. Prescribing and taking medicines. *Brit Med J*. 2003;327(7419):819.
16. Haveman R, Blank R, Moffitt R, Smeeding T, Wallace G. The war on poverty: measurement, trends, and policy. *J Policy Anal Manage*. 2015;34(3):593-638.
17. Anderson TJ, Saman DM, Lipsky MS, Lutfiyya MN. A cross-sectional study on health differences between rural and non-rural U.S. counties using the county health rankings. *BMC Health Serv Res*. 2015;15(441):1-8.
18. Eberhardt MS, Pamuk ER. The importance of place of residence: examining health in rural and nonrural areas. *Am J Public Health*. 2004;94(10):1682-1686.
19. United States Department of Agriculture Economic Research Service. Rural economy and population, 2017. Available at: https://www.ers.usda.gov/topics/natural-resources-environment/. Accessed April 27, 2017.
20. Goeres LM, Gille A, Furuno JP, et al. Rural-urban differences in chronic disease and drug utilization in older oregonians. *J Rural Health*. 2016;32(3):269-279.

21. Weinhold I, Gurtner S. Understanding shortages of sufficient health care in rural areas. *Health Policy*. 2014;118(2):201-214.

22. Goins RT, Williams KA, Carter MW, Spencer M, Solovieva T. Perceived barriers to health care access among rural older adults: a qualitative study. *J Rural Health*. 2005;21(3):206-213.

23. Murphy GK, McAlister FA, Weir DL, Tjosvold L, Eurich DT. Cardiovascular medication utilization and adherence among adults living in rural and urban areas: a systematic review and meta-analysis. *BMC Public Health*. 2014;14:544.

24. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens (Greenwich)*. 2008;10(5):348-354.

25. Krousel-Wood M, Joyce C, Holt E, et al. Predictors of decline in medication adherence: results from the cohort study of medication adherence among older adults. *Hypertension*. 2011;58(5):804-810.

26. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: response to

authors. *J Clin Epidemiol*. 2011;64(3):255-257; discussion 258-263.

27. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res*. 1999;47(6): 555-567.

28. Horne R. Patients' beliefs about treatment: the hidden determinant of treatment outcome? *J Psychosom Res*. 1999;47(6):491-495.

29. Krivoy A, Balicer RD, Feldman B, et al. The impact of age and gender on adherence to antidepressants: a 4-year population-based cohort study. *Psychopharmacology (Berl)*. 2015;232(18):3385-3390.

30. Perreault S, Dragomir A, Roy L, et al. Adherence level of antihypertensive agents in coronary artery disease. *Br J Clin Pharmacol*. 2010;69(1):74-84.

31. Newkirk V, Damico A. The Affordable Care Act and insurance coverage in rural areas, 2014. Available at: http://kff.org/uninsured/issue-brief/the-affordable-care-act-and-insurance-coverage-in-rural-areas/. Accessed May 1, 2017.