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**Risk factors for cost-related medication non-adherence among older patients with diabetes**

Zhang JX *et al*. Cost-related medication non-adherence

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**Abstract**

**AIM:** To assess the risk factors for cost-related medication non-adherence (CRN) among older patients with diabetes in the United States.

**METHODS:** We used data from the 2010 Health and Retirement Study to assess risk factors for CRN including age, drug insurance coverage, nursing home residence, functional limitations, and frequency of hospitalization. CRN was self-reported. We conducted multivariate regression analysis to assess the effect of each risk factor.

**RESULTS:** 875 (18%) of 4,880 diabetes patients reported CRN. Age less than 65 years, lack of drug insurance coverage, and frequent hospitalization significantly increased risk for CRN. Limitation in both activities of daily living and instrumental activities of daily living were also generally associated with increased risk of CRN. Residence in a nursing home and Medicaid coverage significantly reduced risk.

**CONCLUSION:** These results suggest that expanding prescription coverage to uninsured, sicker, and community-dwelling individuals is likely to produce the largest decreases in CRN.

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**Key words:** Cost; Medication; Non-adherence; Risk factors

**Core tip:** Using a nationally representative date set, this study explores a wide range of risk factors influencing cost-related medication non-adherence (CRN), which receives increasing recognition of importance in diabetes. The authors found that age less than 65, lack of prescription drug insurance coverage, increased numbers of hospitalizations, and greater functional limitations were associated with higher likelihood of CRN among diabetic patients, while nursing home residence decreased risk. Together, these results suggest that expanding prescription coverage to uninsured, sicker, and community-dwelling individuals is likely to produce the largest decreases in CRN.

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**INTRODUCTION**

Up to a third of older patients report cost-related medication non-adherence (CRN)[1]. Lower income and high out-of-pocket costs for medications, poorer health status including lower self-perceived general health, more comorbidities, and poorer mental health, are strong risk factors for CRN, while having any, or more generous, prescription drug coverage significantly reduces the risk of CRN[2-6]. Increased costs of prescription drugs are associated with lower rates of medication use, poor health outcomes, more hospitalizations, and increased use of medical services, including emergency department visits[7-9].

There is an increasing recognition of the importance of CRN in diabetes. Diabetic patients often require a large number of prescription drugs and incur high out-of-pocket costs for medications and medical expenses [10, 11]. There is an emerging body of studies examining CRN for diabetes patients, reporting CRN rates ranging from 14% to 30% depending on the study sample[12-17]. However, little is known about the factors associated with CRN in diabetes patients, particularly those who have not yet reached 65 years of age (when they typically become eligible for Medicare), reside in a nursing home, have had multiple hospitalizations, or who have functional limitations. In these patients, medication non-adherence can significantly reduce the effectiveness of care, place them at an increased risk of declining health, and incur significant downstream costs. In addition, several of these risk factors can be potentially modified through social policy and clinical practice. Our aim was to assess variation in CRN with a broad set of risk factors for diabetes patients over the age of 50 using a nationally representative dataset.

**MATERIALS AND METHODS**

***Study population***

We utilized the 2010 data from the Health and Retirement Study (HRS). The HRS is an ongoing longitudinal cross-sectional study that surveys a nationally representative sample of Americans over the age of 50 about their income, employment, health insurance, physical health, cognitive functioning, and health care expenditures[18]. Data for the survey is collected primarily by telephone interview every 2 years. The analysis in this study was restricted to survey respondents who reported that a physician had told them that they had diabetes.

***CRN***

CRN was measured by asking participants, “Sometimes people delay taking medication or filling prescriptions because of the cost. At any time since the last interview or in the last two years have you ended up taking less medication than was prescribed for you because of the cost?” Participants answered either yes or no, although they had the option to refuse to answer or say that they did not know.

***Demographic and socio-economic characteristics***

The HRS includes questions about demographics and socio-economic characteristics, including age, place of birth, education level, ethnicity, employment, and place of residence. We categorized patients into age groups of 50-64 years, 65-74 years, 75-84 years, and 85 years and older. We hypothesized that patients in the age group of 50-64 years old might be at elevated risk of CRN because they may not have had adequate protection from employer-sponsored health insurance and were too young to be eligible for Medicare which could provide low-cost outpatient drug insurance benefits. In addition, depending on the patient’s current health status, it may have been difficult to purchase individual health insurance due to pre-existing conditions.

We included a variable indicating residence in a nursing home. We hypothesized that living in a nursing home and administration of medications by the nursing staff would decrease the risk of CRN. In addition, nursing home patients were more likely to qualify for Medicaid due to low income, and thus out-of-pocket payments for medications should also be reduced, subsequently decreasing the risk of CRN further.

We also included a variable indicating whether the costs of prescription medications were covered at all by health insurance, which may be especially important for low-income persons. We also included a variable indicating patients’ insurance coverage by Medicaid, as Medicaid coverage for the poor may enable their ability to purchase needed drugs.

To describe the resultant burden of out-of-pocket payments for medications with or without medication insurance coverage, we calculated average monthly out-of-pocket expenses for medications, based upon responses to the HRS survey question, “On average, about how much have you paid out-of-pocket per month for these prescriptions since last interview/in the last 2 years?” If they did not know, the interviewer would ask whether it amounted to less or more than a certain dollar amount.

***Functional status and number of hospitalizations***

HRS asks participants about functional status through questions on limitations in activities of daily living (ADLs)[19] and instrumental activities of daily living (IADLs)[20], with higher numbers of limitations indicating worse functional status. Functional limitations may reflect the effects of underlying diseases such as advanced diabetes or other chronic diseases, and can act as barriers to purchasing and administering medications as prescribed.

The HRS also collects information about healthcare utilization, including hospitalizations and physician visits. Participants were asked the number of different times they were hospitalized overnight in the past two years, as well as how many nights they stayed. We hypothesized that while hospitalizations result in out-of-pocket payments that could affect patients’ ability to pay for medications, such effects on CRN might be small given Medicare’s generous coverage for hospitalizations.

We also included an indicator variable for the class of prescription medications each respondent reported taking, including medications for cholesterol, joint or muscle pain, asthma or allergies, stomach problems, insomnia, and anxiety or depression.

***Statistical analysis***

We first performed bivariate analyses of the association between CRN and socio-demographic variables, limitations in ADLs and IADLs, number of hospitalizations, medication insurance coverage, and self-reported monthly out-of-pocket (OOP) payments of prescription drugs. We examined differences in CRN for varying levels of limitations in ADLs and IADLs, medication insurance coverage and socio-demographic variables by utilizing *χ*2 statistics. To evaluate differences in OOP payments for prescription drugs for those with and without CRN, we performed *t*-tests. We then analyzed the association between the number of hospitalizations and CRN by using a general linear regression model, using those without any hospitalizations as the reference group.

We further conducted multivariate regression analysis to assess the net effect of the aforementioned risk factors on CRN. In this case, a logit model was used to assess the independent risk factors including age, nursing home residence, medication insurance coverage, varying level of limitations in ADLs and IADLs, hospitalizations, and medication use for common conditions.

**RESULTS**

Among 22042 respondents in the 2010 HRS, 5037 (23%) reported that they were told by a physician that they had diabetes. The mean age of the 5037 diabetes patients was 67 years (s.d. 11). One-hundred fifty-seven patients (3.1%) were younger than 50 years old and were subsequently excluded from the analysis, resulting in a final sample of 4880 adults. Among the 4880 diabetes patients in the final sample, 875 patients, or 18.3%, reported CRN in the past 2 years.

Of the 875 patients who reported CRN, 573 (65.5%) were between the ages of 50 and 64 years old. Table 1 shows the prevalence of CRN by different socio-demographic variables. Females, African-Americans and Hispanics were more likely to report CRN. As expected, those without any insurance coverage for medications were significantly more likely to report CRN than those with coverage (38% *vs* 16%, *P* < 0.001). There also appeared to be differences in CRN in survey respondents reporting no functional limitations compared to those with 1 or more limitations in ADLs or IADLs, with those with functional limitations more likely to report CRN (25% *vs* 15% for ADLs, *P* < 0.001; 23% *vs* 16% for IADLs, *P* < 0.001). Respondents with at least 1 overnight hospitalization in the past 2 years were also significantly more likely to report CRN compared to those who were never hospitalized (22% *vs* 16%, *P* < 0.001). Nursing home residents had a much lower rate of CRN than community dwellers (5% *vs* 18%, *P* < 0.001). Diabetes patients covered by Medicaid were significantly less likely to report CRN (*P* < 0.001). Respondents who reported CRN had higher monthly out-of-pocket payments for prescription drugs (*P* < 0.001).

Table 2 shows the independent risk factors of CRN in the multivariate logistic regression model. Compared to respondents who were in the 65-74 years age group, those in the age group of 50-64 years were 122% more likely to report CRN. The likelihood of CRN also decreased as patient age advanced. Patients residing in nursing home were 66% less likely to report CRN compared to patients living in the community, and patients without drug insurance coverage were 178% more likely to report CRN compared to those with drug insurance coverage. Patients covered by Medicaid were 66% less likely to report CRN.

Compared to those without any limitations, survey respondents with 1 or more limitations in ADLs or IADLs were much more likely to report CRN, although confidence intervals were wide for the categories with the highest number of limitations so that having 6 or more limitations in ADLs or 3 or more limitations in IADLs were not statistically significant.

Compared to those without any hospitalizations, having any number of hospitalizations increased the risk of CRN. The magnitude of effect on the risk of CRN increased as the number of hospitalizations increased, with a slight decrease for those with 4 or more hospitalizations.

While the coefficients reflecting the effect of each class of medications were all positive in the multivariate logistic regression, in general, they were not statistically significant with the exception of asthma (*P* = 0.007).

**DISCUSSION**

We found that diabetes patients ages 50-64 years old were at increased risk for CRN. A recent report suggests that this age group is at increased risk of being uninsured despite being employed, and due to higher insurance premiums based upon their age and health, it is more difficult for individuals to obtain health insurance elsewhere[21]. That CRN is increased in this age group in our multivariate analysis, which controls for insurance status, suggests that there are other factors besides medication insurance coverage contributing to the higher risk. One factor could be the level of out-of-pocket payments. Although the Affordable Care Act will expand Medicaid eligibility for poor individuals and families, and coverage cannot be denied based on pre-existing conditions, these findings suggest the importance of insurance benefit design so that high-value treatments in diabetes care can be obtained with low out-of-pocket payments. In addition, it is also possible that pent-up demand may be another source of delay in seeking medical care as patients approach the eligibility age of Medicare. Further researches are needed to understand the patient behavior in this aspect.

Our study also found that living in a nursing home is protective for CRN. The high rate of Medicaid coverage among nursing home residents could explain this finding in part as the out-of-pocket payments to medication are nominal for Medicaid beneficiaries. In addition, the administration of medication by the nursing home staff may also reduce the costs of obtaining the medication such as travel, time, and mobility. Overall, Medicaid coverage significantly reduces CRN.

We found the female were more likely to report CRN. Previous researches have reported the gender-specific difference in non-adherence behaviors although the causes of non-adherence were not clear[22,23]. It was possible there was a difference in price-sensitivity to medication between the males and females. This highlighted the need for more researches in the gender difference in CRN in order to increase the adherence.

There was a positive association between CRN and limitations in ADLs and IADLs. This is concerning from a health perspective, since non-adherence may worsen their functional status and their medical disease further. However, the weak evidence for increased CRN among patients with extreme functional limitations in both ADLs and IADLs is notable and surprising. One answer might be that patients who are severely limited in their ability to take care of themselves tend to live in nursing homes and therefore likely to be covered by Medicaid, so that CRN is rare. However, we control for both these factors in our analysis. Another possibility is that the dependency of these individuals prompts others to provide them with assistance in obtaining medications that makes cost less of a barrier. However, this is purely speculative and this result seems worthy of further analysis.

The positive correlation between CRN and the number of hospitalizations is notable because non-adherence can potentially increase the likelihood of readmission, thus driving more expensive care. It is less clear from the data available whether the number of hospitalizations increases CRN, CRN increases hospitalization rates, or both. Future research should be directed at assessing the causal relationship between hospitalizations and CRN in such a high-risk patient population.

This study is limited in that while we have shown that a number of factors may be affecting CRN, we do not have measures of some key factors, such as insurance benefit design. As a result, the exact reason for CRN among those with drug insurance coverage is less clear. Also, the HRS survey does not give us any indication of how often participants did not take their medications due to cost, and only asks whether they had done so within the past 2 years.

Diabetes is a major chronic condition that causes significant mortality and morbidity, requiring coordination of care to treat the patient as a whole person[24]. It is a disease in which patient nonadherence to medications may be a result of a number of failures in social, economic, behavioral, and managerial aspects of care. Previous research suggests that insurance coverage alone does not guarantee high quality of diabetes care to patients[25], and more research is much needed to understand the influence of the hybrid of factors influencing CRN, in order to prevent the well-known complications of the disease that can debilitate patients further in the future.

In conclusion, despite the limitations of the study, the results imply that there are significant opportunities to reduce CRN and improve the effectiveness of pharmacotherapy in diabetes patients through public policy and clinical practice. More research is needed to elucidate the causal relationship between functional limitations, hospitalizations, and CRN. In addition, interventions that aim to reduce cost-cutting behaviors such as generic medication substitution in these patients have the potential of improving the effectiveness of treatment and reducing overall medical costs.

**COMMENTS**

***Background***

There is an increasing recognition of the importance of cost-related medication non-adherence (CRN) in diabetes. However, little is known about the factors associated with CRN in diabetes patients, particularly those who have not yet reached 65 years of age, reside in a nursing home, have had multiple hospitalizations, or who have functional limitations.

***Research frontiers***

Researches have shown that lower income and high out-of-pocket costs for medications, poorer health status including lower self-perceived general health, more comorbidities, and poorer mental health, are strong risk factors for CRN, while having any, or more generous, prescription drug coverage significantly reduces the risk of CRN. Increased costs of prescription drugs are associated with lower rates of medication use, poor health outcomes, more hospitalizations, and increased use of medical services, including emergency department visits

***Innovations and breakthroughs***

Using a nationally representative sample, the authors evaluated an array of risk factors of CRN including pre-Medicare (65 years old), residence status in nursing home, repeated hospitalizations, and functional limitations.

***Applications***

These results suggest that expanding prescription coverage to uninsured, sicker, and community-dwelling individuals is likely to produce the largest decreases in CRN.

***Terminology***

CRN: cost-related medication non-adherence.

***Peer review***

The authors conclude that expanding prescription coverage to uninsured, sicker, and community-dwelling individuals is likely to produce the largest decreases in CRN. The findings are interesting.

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**Table 1 Prevalence of cost-related medication non-adherence by Socio-Demographics, Health Status and Usage of Medical Resources *n* (%)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | All | Reported CRN | Did not report CRN | *P* value |
| Full sample | 4880 (100) | 875 (18) | 4005 (82) |  |
| Age |  |  |  |  |
| ≥ 50 and ≤ 64 | 2031 (100) | 573 (28) | 1458 (72) | < 0.001 |
| ≥ 65 and ≤ 74 | 1505 (100) | 207 (14) | 1298 (86) |
| ≥ 75 and ≤ 84 | 1017 (100) | 82 (8) | 935 (92) |
| ≥ 85 | 329 (100) | 13 (4) | 314 (96) |
| Gender |  |  |  |  |
| Male | 2224 (100) | 343 (15) | 1881 (85) | < 0.001 |
| Female | 2656 (100) | 532 (20) | 2124 (80) |
| Race |  |  |  |  |
| White | 3298 (100) | 502 (15) | 2796 (85) | < 0.001 |
| African-American | 1187 (100) | 277 (23) | 910 (77) |
| Other | 393 (100) | 94 (24) | 299 (76) |
| Ethnicity |  |  |  | 0.003 |
| Hispanic | 883 (100) | 189 (21) | 694 (79) |
| Non-Hispanic | 3997 (100) | 686 (17) | 3311 (83) |
| Nursing Home |  |  |  |  |
| Living in NH | 138 (100) | 7 (5) | 131 (95) | < 0.001 |
| Not in NH | 4742 (100) | 868 (18) | 3874 (82) |
| Insurance coverage for Rx |  |  |  |  |
| Yes | 4461 (100) | 716 (16) | 3745 (84) | < 0.001 |
| No | 419 (100) | 159 (38) | 260 (62) |
| Medicaid coverage |  |  |  |  |
| Currently covered | 349 (100) | 24 (7) | 325 (93) | < 0.001 |
| Not covered | 4531 (100) | 851 (19) | 3680 (81) |
| ADL limitations |  |  |  |  |
| No limitation | 3455 (100) | 519 (15) | 2936 (85) | < 0.001 |
| 1 or more limitations | 1425 (100) | 356 (25) | 1069 (75) |
| IADL limitations |  |  |  |  |
| No limitation | 3442 (100) | 547 (16) | 2895 (84) | < 0.001 |
| 1 or more limitations | 1438 (100) | 328 (23) | 1110 (77) |
| Hospitalization |  |  |  |  |
| No hospitalization | 3081 (100) | 486 (16) | 2595 (84) | < 0.001 |
| 1 or more hospitalizations | 1799 (100) | 389 (22) | 1410 (78) |
| Monthly out-of-pocket payments for Rx |  |  |  |  |
| Payments: $ (s.d.) | 69 (2.4) | 108 (6.9) | 60 (2.5) | < 0.001 |

*P* values by *χ*2 tests, except for out-of-pocket payments for Rx, where *t*-test was performed. CRN: Cost-related medication non-adherence; ADL: Activities of daily living; IADL: Instrumental activities of daily living.

**Table 2 Results of Multivariate Logistic Regression Analysis of Medication cost-related medication non-adherence**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Odds ratio | P>z | 95%CI |
| Age |  |  |  |
| Age 50-64 | 2.182 | 0.000 | 1.805-2.638 |
| Age 65-74 | Reference | - | - |
| Age 75-84 | 0.532 | 0.000 | 0.403-0.704 |
| Age 85+ | 0.236 | 0.000 | 0.131-0.426 |
| Residence |  |  |  |
| Nursing home residence | 0.335 | 0.011 | 0.145-0.775 |
| Medicare insurance coverage |  |  |  |
| No drug coverage | 2.824 | 0.000 | 2.233-3.570 |
| Medicaid coverage |  |  |  |
| Currently covered by Medicaid | 0.341 | 0.000 | 0.217-0.535 |
| Functional limitations |  |  |  |
| Activities of daily living |  |  |  |
| No limitation | Reference | - | - |
| 1 limitation | 1.431 | 0.005 | 1.113-1.840 |
| 2 limitations | 1.850 | 0.000 | 1.348-2.540 |
| 3 limitations | 1.813 | 0.003 | 1.229-2.674 |
| 4 limitations | 1.796 | 0.012 | 1.137-2.838 |
| 5 limitations | 1.776 | 0.023 | 1.083-2.911 |
| 6 limitations | 1.669 | 0.162 | 0.813-3.425 |
| Instrumental activities of daily living |  |  |  |
| No limitation | Reference | - | - |
| 1 limitation | 1.376 | 0.006 | 1.094-1.731 |
| 2 limitations | 1.494 | 0.014 | 1.084-2.060 |
| 3 limitations | 1.243 | 0.307 | 0.819-1.887 |
| 4 limitations | 0.872 | 0.651 | 0.482-1.579 |
| Number of hospitalizations |  |  |  |
| No hospitalization | Reference | - | - |
| 1 hospitalization | 1.320 | 0.010 | 1.068-1.632 |
| 2 hospitalizations | 1.437 | 0.011 | 1.089-1.898 |
| 3 hospitalizations | 1.683 | 0.005 | 1.168-2.424 |
| 4 or more hospitalizations | 1.507 | 0.013 | 1.091-2.082 |
| Medication use for common conditions |  |  |  |
| Cholesterol | 1.118 | 0.202 | 0.942-1.327 |
| Pain | 1.090 | 0.320 | 0.942-1.327 |
| Asthma | 1.295 | 0.011 | 1.062-1.578 |
| Stomach | 1.141 | 0.186 | 0.939-1.388 |
| Sleep | 1.077 | 0.516 | 0.861-1.347 |
| Anxiety | 1.082 | 0.453 | 0.880-1.330 |

Results from multivariate logistic regression analysis.