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The Paradox of Decreasing Rates of Cost-Related Medication Non-Adherence Among Old and Older-Old Americans: A Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-051480
Article Type:	Original research
Date Submitted by the Author:	20-Mar-2021
Complete List of Authors:	Zhang, James; The University of Chicago, Medicine; 5841 S Maryland Ave. Bhaumik, Deepon Meltzer, David; The University of Chicago
Keywords:	Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH

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3 **The Paradox of Decreasing Rates of Cost-Related Medication Non-Adherence Among Old and**
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5 **Older-Old Americans: A Longitudinal Study**
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33 Total number of words: 3,115

34 Running title: Aging and cost-related medication non-adherence

35
36 Key words: cost-related medication non-adherence, aging, paradox
37
38

39 Total number of tables: 3

40
41 Total number of Figures: 3
42
43
44

45 ACKNOWLEDGEMENT

46
47 The study was presented in part at the International Health Economics World Congress, Basel,

48
49 Switzerland, July 16, 2019. This study is supported in part by Chicago Center for Diabetes

50
51 Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30 DK092949), and

52
53 NIH 5R21AG053749 (Meltzer & Zhang).
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Abstract**(280 words)**

Objectives: The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. Cost-related medication non-adherence (CRN) is an important measure of medication non-adherence behaviors that aim to avoid costs. While there is an emerging body of literature on the cross-sectional analysis of CRN internationally, longitudinal study of CRN behaviors for the aging population is rare.

Design: Longitudinal study using the Health and Retirement Study to evaluate self-reported CRN biennially.

Setting: General population of older Americans.

Participants: Two cohorts of Americans aged between 50 and 79 (old) and 80 or above (older-old) followed from 2004 to 2014.

Intervention: Observational with no intervention.

Primary and secondary outcome measures: Using multivariable regression analyses controlling for a broad set of variables including socio-demographics, Social Security (SS) income to total income ratio, functional status, and comorbid conditions, we evaluated population-adjusted CRN over time, including comparison of CRN rates between those who were alive and those who were deceased during the follow-up.

Results: The two old and older-old cohorts with 13,254 and 9,856 respondents represented 57.5 million and 7.7 million people in 2004, respectively. Decreasing CRN was observed in both old and older-old cohorts despite their decreasing income, increasing SS income to total income ratio, and increasing limitations in the functional status and disease burden measured by comorbidities. Those who were deceased had reported lower prevalence rates but higher intensity of CRN.

Conclusion: The paradox of lower CRN with less economic resources and higher disease burden suggests patient's CRN behaviors change as they age. Further research in social policy is greatly need to address the basic needs of the elderly and improve their overall well-being.

Summary

Strength of the study:

- Nationally representative study sample
- Longitudinal follow-up of CRN which is rare in the literature
- Population-adjusted CRN rates for direct comparison
- Further comparison of CRN rates between those who were alive and who were deceased during the follow-up

Weakness of the study

- Does not have information in change in the consumption bundle such as the other discretionary spending over time.

Introduction

The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. A recent national poll indicated that among those currently taking prescription drugs, one-fourth of adults (24 percent) and seniors (23 percent) have difficulty in affording their prescription drugs including about one in ten (overall and among seniors) saying it is “very difficult.”¹ Cost-related medication non-adherence (CRN) is a metric measuring such cost-avoiding behaviors and has seen an emerging body of literature on its prevalence internationally. For example, in a study of adults aged 55 and older and living in the community in 11 developed countries, the authors found that following the lead of the U.S. with 16.8% in CRN to medication, Canada had the second highest national prevalence of CRN (8.3%), followed by Australia (6.8%).² Many patients engage in strategies to avoid such costs when facing difficult choices between their medication needs and other basic needs, including delaying filling prescription, not filling prescriptions, skipping doses and splitting doses. Many behavioral, social, economic, medical, and policy-related factors have been identified as contributing factors for medication non-adherence.³⁻⁵ Medication non-adherence is associated with increased hospitalization rates and emergency department visits, higher mortality rates, worse patient outcomes, and increased downstream costs that impose heavy, avoidable healthcare costs on society.⁶⁻¹¹ Hence it is pressing for researchers, practitioners, and policy makers to gain insight into the key factors that drive the difference in CRN across population strata.

Among the many risk factors for CRN, age receives little attention even though younger disabled patients have been found to have higher CRN rates among the Medicare population.¹² In essence, age is a complex variable reflecting multiple dimensions of biological and social factors that can potentially drive-up CRN. For example, since older people may have protection

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3 from the Medicare insurance coverage including Part D outpatient prescription drug program,
4 and at the same time, older people also have lower income and may suffer from multiple chronic
5 conditions which require greater out-of-pocket spending on medications, and thus the tension
6 between their resources and medication needs is relatively higher. The literature on the effect of
7 aging process on CRN is scant, and most reported differences in CRN due to age is examined in
8 the context of cross-sectional studies, which makes it unclear if the age difference in CRN is due
9 to generational difference (i.e., cohort effect) or the aging process itself and also lacks of
10 adequate control for the confounding factors. It is important to study the effects of the aging
11 process on CRN because if the older people with less economic resource and higher disease
12 burden reported lower CRN rates, *ceteris paribus*, it may mean they are actually cutting down
13 spending on other basic needs and that therefore social policy may need to be revamped to
14 address this hidden crisis. On the other hand, this is an interesting question about the behavioral
15 change in the aging process, as it may reflect the change in the assessment of the value of
16 medication (and life) as people progress to more advanced age.

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18 We hence propose to study the CRN behaviors among the older population in the US
19 longitudinally with a broad set of variables to control for potential confounders. The longitudinal
20 analysis isolates the cohort effect from its tempering of the age effect, and the broad set of
21 controlling variables (particularly income) further isolate the potential confounding. We used the
22 Health and Retirement Study (HRS), a nationally representative sample of older people (50 years
23 or older) to generate population-adjusted estimates for the whole nation.

24 **Methods**

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26 Data from HRS from 2004 to 2014 were used for this study. The HRS is a longitudinal
27 panel study that surveys a representative sample of Americans over the age of 50 about their

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3 income, employment, health insurance, physical health, functional status, and medical
4 conditions.¹³ Data for the survey is collected primarily by telephone interview every 2 years.
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6 Mortality was recorded if the respondent was deceased during the follow-up.
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10 CRN was measured by asking participants, “Sometimes people delay taking medication or
11 filling prescriptions because of the cost. At any time since the last interview or in the last two
12 years have you ended up taking less medication than was prescribed for you because of the
13 cost?” Participants answered either yes or no, although they had the option to refuse to answer or
14 say that they did not know. For those who refused to answer or say that they did not know, the
15 answer is treated as no CRN was reported.
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24 We created two cohorts with age between 50 and 79 (old) and 80 or above (older-old) in
25 2004 and followed them to 2014 and evaluated population-adjusted CRN over time. The reason
26 for creating two cohorts is to isolate the generational difference in CRN behaviors at baseline,
27 and to compare the trajectory of CRN behaviors in these two cohorts by controlling other
28 confounding factors. Such a grouping is also consistent with the older population defined by the
29 US Census.¹⁴ The reason for the follow-up between 2004 and 2014 is that although the two
30 cohorts experienced the Great Recession starting in 2008, the economy had largely recovered in
31 steady growth by 2014 and hence this period of 10 years provides a clear picture of the trajectory
32 of CRN pre-, during, and post-economic recession with up to six observations for each
33 correspondent. To generate population-adjusted CRN rates at each of six survey rounds between
34 2004 and 2014, we performed the analysis as follows:
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49 We developed multiple logistic regression models to obtain the population-adjusted CRN
50 rates for each of the survey rounds between 2004 and 2014 by controlling a wide range of
51 covariates. These covariates included socio-demographics including age, gender, race, and
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3 ethnicity. Since insurance status has been found an important predictor for CRN and the
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5 overwhelming majority of the elderly (65 years of old) have Medicare as their primary insurer,¹⁵
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7 we included an indicator variable for those who were enrolled in Medicaid. An enrollment in
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9 Medicaid would indicate that they were at the lowest economic ladder since Medicaid is a
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11 means-tested state-sponsored public insurance program for those who meet the poverty level
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13 defined by each state. Research has also shown those with Medicare-Medicaid dual eligibility
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15 (dual eligible) can have high CRN rates despite the additional insurance coverage, likely due to
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17 the fact that those at the bottom of economic ladder are highly sensitive to the out-of-pocket
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19 payment.¹⁶ Hence we think the inclusion of both income variable and Medicaid coverage will
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21 tease out two different confounding: one on the resource availability, the other on the enabling
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23 effect of health insurance to overcome such resource limitation but with certain behaviors traits
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25 such as price sensitivity. We also included two variables on functional status: limitations in
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27 Activities of Daily Living (ADLs), and Instrumental Activities of Daily Living (IADLs).^{17,18}
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29 These two variables measure the number of limitations in performing tasks such as dressing,
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31 bathing, eating, toileting, getting out of bed, and walking (ADLs), and preparing meals,
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33 shopping, managing money, and taking phone calls (IADLs). Research has also that functional
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35 status is an important factor reflecting the out-of-pockets for medical care as they reflect the
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37 heightened frailty and increased costs to visit physicians and obtaining medications.¹⁹ We also
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39 included a set of comorbid conditions including diabetes, heart disease, stroke, and cancer. These
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41 conditions are known to have high disease burden for patients in terms of both the need for
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43 continuous medical care and high costs of medication treatments.¹⁵
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51 In addition, we created a new variable for the ratio of social security (SS) to total income in
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53 order to further isolate the effect of income on CRN from potential confounding. HRS has a rich
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3 set of questionnaires on sources of income and given that many of the elderly are already in
4 retirement and wage income would have been a poor proxy, we first created one variable for
5 total income, including wages, pensions, unemployment benefits, SS income, and income from
6 investments and financial assets for each patient. (See Appendix I for a list of sources of
7 income). Because not every income-related variable is measured on a monthly basis, we
8 extrapolated these variables to its annual amount. We then created a variable indicating the ratio
9 of SS income to total income. We think while the total income reflects the total resources
10 available to the patients in absolute term, it's highly skewed and does not necessarily reflect the
11 resource constraints which are more pertinent to the old people who are living on fixed income
12 such as Social Security, the SS-income ratio better reflects the degree to which the respondent
13 relies on SS income for their daily lives in a relative term. Research showed that in 2013,
14 Medicare beneficiaries' average out-of-pocket health care spending was 41 percent of average
15 per capita SS income,²⁰ suggesting the importance to use SS income as a benchmark for the
16 resource availability for the elderly on the population level. We think that the higher SS-income
17 ratio would indicate smaller room for trade-off between the medication needs and other daily
18 needs as the respondents have no other economic resources to turn to once they use up the SS
19 income, which is often too low to sustain a life given all of their disease burdens.

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22 To further ascertain the difference between those who were deceased and alive during the
23 follow-up periods, we conducted the multiple regression analyses by examining two composite
24 CRN variables: one for "any" CRN during the follow-up period; the other for average times the
25 respondent reported CRN given the follow-up span when the respondent was alive, where the
26 numerator was the sum of the number of times a respondent responded "Yes" to CRN, and the
27 denominator was equal to a count of the number of years the respondent was alive/participated in

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3 the study. For example, if a respondent indicated “YES” only for 2004 and 2010 and was alive
4 for every survey for a total of 6 surveys between 2004 and 2014, the average CRN is 2/6, which
5 is 0.33 (or 33% of time). If the respondent were deceased before 2012, for the same two “YES”
6 for 2004 and 2010, the average CRN would be 2/4, which is 0.5 (or 50% of time). We think the
7 measure of “any” shows the prevalence of CRN during the follow-up period for the ceiling of the
8 such behavior, and the measure of “average CRN” shows the intensity of such behaviors during
9 the same time period.

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11 We compared the demographic variables, Medicaid enrollment, and comorbid conditions for
12 each cohort at 2004 and 2014 respectively, using Chi-squared tests. We compared the number of
13 functional status between 2004 and 2014 for the two cohorts using t-tests. All analyses were
14 weighted to reflect the population average. Finally, to compare the change in the average effect
15 size for each of the aforementioned variables in influencing CRN, we conducted multiple logistic
16 regression analyses by pooling the respondents in two cohorts and estimating their adjusted odds
17 ratio for 2004 and 2014, respectively.

18 Patient and Public Involvement

19 No patient involved.

20 Results

21 Table 1 shows the demographics, income, Medicaid enrollment status, functional status, and
22 comorbid conditions at the baseline of 2004 and at the end of follow-up of 2014, for the two old
23 and older-old cohorts, with 13,254 and 9,856 respondents representing 57.5 million and 7.7
24 million people at the baseline, respectively. All respondents 50 years or old in the HRS were
25 included. After 10 years, 9,856 and 529 patients remained alive in the two cohorts representing
26 45.2 and 1.82 people at 2014 after ascertaining death recorded in the HRS. The unadjusted CRN

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3 prevalence rates were 10.4% and 4.6% at 2004, and decreased to 7.31% and 2.6% in 2014, for
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5 the old and older-old cohorts, respectively. The adjusted CRN prevalence rates were 8.5% and
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7 5.9% at 2004, and decreased to 4.5% and 1.3%, for the old and older-old cohorts, respectively.
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10 There were significant changes in patient mix in both cohorts over time. The survivors appeared
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12 to be more likely to have high education degree, and Medicaid coverage. Overall, the functional
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14 limitations in both ADLs and IADLs, and the prevalence of comorbid conditions by four
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16 conditions increased in both cohorts.
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19 Table 2 shows the population-average adjusted odds ratio (AOR) of variables in affecting CRN
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21 by pooling the two cohorts for the year of 2004 and 2014. The AOR of female sex decreased
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23 from 2.18 to 1.65 from 2004 to 2014; and during this time period, the AOR of high school
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25 degree increased from 0.90 to 1.26, the AOR of diabetes increased from 1.14 to 1.54, among
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27 other changes.
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30 Table 3 shows the CRN prevalence rate by “any” CRN and percentage of time of CRN was
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32 reported during the follow-up when the respondent was alive. For the old cohort, 27.2% of those
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34 who survived had at least reported CRN at least once, and 21.2% of those who were deceased
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36 had reported CRN at least once. In contrast, the average percentage of time when a CRN was
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38 reported across 6 surveys between 2004 and 2014 was 9.2 for those who survived, and 10.8 for
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40 those who were deceased. A similar pattern was observed for the older-old cohort.
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44 Figure 1 shows the population-adjusted CRN rates by age cohort from 2004 to 2014. There was a
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46 general downward trend in both age cohort, despite a small bump between 2008 and 2012 when
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48 the economy was in turmoil due to the Great Recession.
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51 Figure 2 shows the trend of ratio of SS income to total income by age cohort from 2004 to 2014.
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54 While the older-old cohort has a steady ratio over time, there was a clear upward trend among
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3 the old cohort, with the slope becoming steeper during 2010-2012 period, and then flattening out
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5 during 2012-2014.
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8 Figure 3 shows the trend of total income by age cohort from 2004 to 2014. While the older-old
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10 cohort remained largely stable over this period, there was a significant drop of income in the old
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12 cohort between 2006 and 2012 which flattened out in 2014.
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14 **Discussion and Conclusions**

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17 There was a clear downward trend in the CRN prevalence rates in both old and older-old
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19 cohorts between 2004 and 2014, despite economic downturn after 2008 due to the Great
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21 Recession. The younger cohort of those 50-79 suffered significantly in terms of loss of income
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23 during this time period, and their SS income to total income ratio increased, reflecting their
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25 increasing dependence on the SS income and decreasing economic resources available to them
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27 over time. Despite such decreasing economic resources for this group and high dependence on
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29 SS income for both cohorts, the population-adjusted CRN rates steadily decreased.
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34 Such a steady decrease in CRN rates was accompanied by increasing limitations in functional
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36 status in both ADLs and IADLs and increasing prevalence of comorbid conditions, reflecting
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38 heightened frailty and disease burden in both cohorts as they aged. There was an increase in the
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40 Medicaid enrollment in both cohorts in both cohorts, which likely provides protection from
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42 CRN. However, even after adjusting for Medicaid enrollment, the clear pattern of decreasing
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44 CRN is still seen as the population ages.
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48 Such a pattern of decreasing CRN as the population ages could not explained away by the
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50 fact of that a significant fraction of the elderly were deceased during the follow-up. As we have
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52 shown, the CRN prevalence rates among the survivors were actually higher than those who were
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3 decreased, even though the intensity of CRN was higher among those who were deceased, likely
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5 reflecting the struggle during the last few years of life.
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8 Hence such a “paradox” of lower CRN rates among the old Americans with decreasing
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10 economic resources but higher disease burden which require higher consumption of medications
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12 seems to be robust, persisting through a series of controls for confounding factors. One possible
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14 explanation is that as the population ages and faces a shorter remaining life-span, the valuation of
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16 the worthiness of medication may change, rendering the population to change their consumption
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18 bundle with more resources devoted to the medication use. Because the elderly population is
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20 increasingly dependent on their fixed SS income, such a change in their consumption bundle will
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22 inevitably decrease their ability to afford other daily needs, such as housing, food, and
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24 transportation. There is little literature in this aspect of the loss of welfare due to the pressure to
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26 pay for the medications. More research is greatly needed to evaluate the adequacy of social
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28 policy to help the elderly cope with increasing demand for medications as they age. When CRN
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30 was examined longitudinally, one recent study suggested that younger age is a risk factor for
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32 persistent CRN.²¹ The evidence from this study corroborates that patient’s behavior may evolve
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34 when they age.
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40 It is also noteworthy that those who were deceased had lower CRN prevalence overall but
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42 higher intensity of CRN compared to those who survived the 10 years of follow-up through the
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44 economic downturn. The lower CRN prevalence may suggest that it may not be that CRN caused
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46 higher mortality overall, and the heightened intensity of CRN may reflect increased financial
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48 struggle due to the increasing disease burden as individuals approach the end of their life. In
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50 other words, this additional evidence is in line with the thought that those who approach end-of-
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3 life have higher resource utilization, but this does not affect the general trend that aging process
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5 render the elderly less likely to report CRN.
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8 This study is limited by the fact that the HRS does not have data to examine the subjective
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10 evaluation of consumption bundles in order to derive the exact cause of decreasing CRN despite
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12 increasing disease burden and decreasing economic resources. Nor does the HRS allows an
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14 exhaustive examination of consumption by goods and services. Future research should be
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16 directed to examine these issues and to further illuminate the changing consumption preferences
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18 of the elderly. Needless to say, such a change is forced upon them when the elderly are faced
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20 with decreasing economic resources at the same time as higher disease burdens. Further
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22 understanding of the coping mechanisms and trade-offs faced by the elderly may have profound
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24 implications for social policy that aims to protect the elderly.
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28 In summary, we presented a clear case of decreasing CRN rates among the old and older-old
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30 cohorts despite decreasing economic resources, increasing disease burden, and increasing
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32 Medicaid coverage. Such a paradox is possibly driven by the change in preferences for
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34 medication or the perceived value of medications as the population ages. This may suggest a
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36 hidden gap in social policy as the elderly cope with increased burdens by reducing consumption
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38 of other goods and services which may reduce their overall well-being. More research is greatly
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40 needed to understand this phenomenon and improve social policy for our aging population.
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ACKNOWLEDGEMENT

The study was presented in part at the International Health Economics World Congress, Basel, Switzerland, July 16, 2019. This study is supported in part by Chicago Center for Diabetes Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30 DK092949), and NIH 5R21AG053749 (Meltzer & Zhang).

AUTHOR CONTRIBUTIONS

Dr Zhang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Zhang.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Zhang.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Bhaumik, Zhang.

Obtained funding: Meltzer, Zhang.

Administrative, technical, or material support: Meltzer, Zhang.

Supervision: Zhang.

Conflict of Interest Disclosures: Dr Meltzer reported receiving compensation from CVS Consultant outside the submitted work. No other disclosures were reported.

ETHICAL APPROVAL / PATIENT CONSENT

The public use file of the Health and Retirement Study does not have human subjects, hence patient consent or the approval by the Institutional Review Board is not required.

DATA SHARING STATEMENT

The public use file of the Health and Retirement Study can be downloaded directly from its webpage accessible at <https://hrs.isr.umich.edu/about>.

REFERENCES

1. Kaiser Family Foundation. KFF Health Tracking Poll – February 2019: Prescription Drugs. 2019. Available <https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/>. Accessed August 14, 2020.
2. Morgan SG, Lee A. Cost-related non-adherence to prescribed medicines among older adults: a cross-sectional analysis of a survey in 11 developed countries. *BMJ Open* 2017;7:e014287.
3. Gellad WF, Grenard J, McGlynn EA. A review of barriers to medication adherence: a framework for driving policy options. RAND Corporation, 2009. Available at: http://www.rand.org/pubs/technical_reports/TR765.html. Accessed March 1, 2019.
4. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004; 42:200-9.
5. National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan. 2007. Available at http://www.talkaboutrx.org/documents/enhancing_prescription_medicine_adherence.pdf. Accessed February 4, 2017.
6. Tamblyn R, Laprise R, Hanley JA, Abrahamowicz M, Scott S, Mayo N, Hurley J, Grad R, Latimer E, Perreault R, McLeod P, Huang A, Larochelle P, Mallet L Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001; 285:421–429.
7. Mojtabai R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff*. 2003; 22(4):220–229.
8. Heisler M, Langa KM, Eby EL, Fendrick AM, Kabeto MU, Piette JD. The health effects of restricting prescription medication use because of cost. *Med Care*. 2004; 42:626–634.
9. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006; 166:1836–1841.
10. Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ, Krumholz HM, Rumsfeld JS. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Arch Intern Med*. 2006; 166:1842–1847.
11. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014 Feb 20; 7:35-44.
12. Soumerai SB, Pierre-Jacques M, Zhang F, et al. Cost-related medication nonadherence among elderly and disabled Medicare beneficiaries: a national survey 1 year before the medicare drug benefit. *Arch Intern Med*. 2006;166(17):1829-1835.
13. The Health and Retirement Study. Available <https://hrs.isr.umich.edu/about>. Accessed August 20, 2020.
14. The US Census. The Older Population in the United States: 2004. Available <https://www.census.gov/data/tables/2004/demo/age-and-sex/2004-older-population.html>. Accessed August 24, 2020.
15. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med*. 2007;22(6):864-71.

16. Zhang JX, Meltzer DO. The High Cost-related Medication Non-adherence Rate Among Medicare-Medicaid Dual-Eligible Diabetes Patients. *J Health Med Econ.* 2016;2(2).
17. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. the index of adl: a standardized measure of biological and psychosocial function. *Journal of American Medical Association.* 1963; 185:914-919.
18. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist.* 1969;9(3):179-186.
19. Zhang JX, Lee JU, Meltzer DO (2015) The Effect of Functional Limitations and Hospitalization on Out-of-Pocket Medical Payments in older Adults. *Ann Community Med Pract* 1(1): 1004.
20. Kaiser Family Foundation. Medicare Beneficiaries' Out-of-Pocket Health Care Spending as a Share of Income Now and Projections for the Future. 2018. Available <https://www.kff.org/medicare/report/medicare-beneficiaries-out-of-pocket-health-care-spending-as-a-share-of-income-now-and-projections-for-the-future/>. Accessed August 24, 2020.
21. De Avila JL, Meltzer DO, Zhang JX. Prevalence and Persistence of Cost-Related Medication Nonadherence Among Medicare Beneficiaries at High Risk of Hospitalization. *JAMA Netw Open.* 2021;4(3):e210498. doi:10.1001/jamanetworkopen.2021.0498

Table 1. Socio-economic and health characteristics of the study sample.

	Age 50-79 in 2004		P-value	Age ≥ 80 in 2004		P-value
	2004	2014		2004	2014	
Total N: sample (weighted)	13,254 (57,522,395)	9,856 (45,250,407)		2,666 (7,709,927)	529 (1,856,348)	
CRN (% of total)	10.42	7.31	<0.001	4.64	2.6	<0.001
Population-adjusted CRN (% of total)	8.5	4.5		5.9	1.3	
Demographics						
Mean Age (SD)	62.3 (8.2)	70.9 (7.7)	<0.001	84.6 (3.9)	92.8 (2.6)	<0.001
Male N (%)	26,537,035 (46.13)	19,959,531 (44.11)	<0.001	2,865,953 (37.17)	549,748 (29.61)	<0.001
Race						
White N (%)	46,566,916 (81.0)	36,778,482 (81.3)	<0.001	6,722,307 (87.2)	1,648,583 (88.8)	<0.001
Black N (%)	5,422,810 (9.4)	3,946,334 (8.7)	<0.001	563,630 (7.3)	123,727 (6.7)	<0.001
Other N (%)	1,533,962 (2.7)	1,299,172 (2.9)	<0.001	82,439 (1.1)	13,734 (0.7)	<0.001
Hispanic N (%)	1,498,296 (7.0)	3,218,998 (7.1)	<0.001	341,551 (4.4)	70,304 (3.79)	<0.001
High School Degree N (%)	44,792,359 (78.1)	36,771,098 (81.6)	<0.001	5,104,259 (66.2)	1,382,472 (74.5)	<0.001
Mean Social Security to Income Ratio (SD)	0.61 (0.34)	0.70 (0.34)	<0.001	0.72 (0.32)	0.72 (0.33)	<0.10
Medicaid Only N (%)	4,347,512 (7.57)	4,195,261 (9.34)	<0.001	741,106 (9.68)	376,197 (20.77)	<0.001
Functional status						
Activities of Daily Life N (SD) (dress, bath, walk, eat, bed, toilet)	1.11 (1.93)	1.20 (1.97)	<0.001	1.36 (1.94)	2.19 (2.27)	<0.001
Instrumental Activities of Daily Life N (SD) (meal, shop, phone, money)	0.24 (0.65)	0.35 (0.86)	<0.001	0.85 (1.24)	1.82 (1.65)	<0.001
Comorbid condition						
Cancer N (%)	6,729,897 (11.8)	8,279,802 (18.5)	<0.001	1,601,000 (21.1)	463,700 (25.4)	<0.001
Diabetes N (%)	9,870,732 (17.3)	11,607,147 (25.9)	<0.001	1,268,614 (16.8)	387,277 (21.2)	<0.001
Heart Condition N (%)	11,463,265 (20.07)	12,694,226 (28.3)	<0.001	3,141,721 (41.5)	897,113 (49.21)	<0.001
Stroke N (%)	2,981,224 (5.2)	3,558,686 (7.94)	<0.001	972,042 (12.8)	392,876 (21.6)	<0.001

Legend: the numbers were weighted using 2004 HRS sample weight except the first row representing the sample.

Table 2. Adjusted Odd Ratio from Multivariate Logit Models of CRN, 2004 and 2014

	2004				2014			
	Odds Ratio	Standard Error	P-Value	95% CI	Odds Ratio	Standard Error	P-Value	95% CI
Age Group	0.51	0.09	0.00	0.35, 0.73	0.27	0.07	0.00	0.16, 0.46
Sex (Female)	2.18	0.31	0.00	1.61, 2.95	1.65	0.19	0.00	1.28, 2.11
Race (White)	Referent	-	-	-	-	-	-	-
Race (Black)	2.00	0.22	0.00	1.59, 2.52	2.09	0.22	0.00	1.67, 2.61
Race (Other)	0.61	0.21	0.16	0.3, 1.25	0.68	0.23	0.27	0.34, 1.38
Hispanic	1.37	0.12	0.00	1.14, 1.66	2.55	0.33	0.00	1.94, 3.35
High School Diploma	0.90	0.10	0.33	0.71, 1.13	1.26	0.19	0.15	0.91, 1.75
Social Security Income Ratio	1.99	0.19	0.00	1.63, 2.43	3.18	0.63	0.00	2.09, 4.83
Medicaid	0.95	0.19	0.81	0.62, 1.45	0.87	0.22	0.60	0.51, 1.5
ADL	0.99	0.02	0.70	0.96, 1.03	0.98	0.05	0.61	0.88, 1.08
IADL	1.12	0.04	0.00	1.05, 1.2	0.99	0.06	0.93	0.87, 1.14
Diabetes	1.13	0.11	0.22	0.92, 1.39	1.54	0.13	0.00	1.28, 1.84
Stroke	1.44	0.11	0.00	1.24, 1.68	0.95	0.40	0.91	0.39, 2.34
Heart Disease	1.42	0.06	0.00	1.3, 1.56	1.65	0.21	0.00	1.27, 2.15
Cancer	0.87	0.07	0.12	0.73, 1.04	0.74	0.19	0.27	0.43, 1.29
Constant	0.03	0.01	0.00	0.02, 0.04	0.01	0.00	0.00	0.01, 0.01
C-Statistic	0.68	-	-	-	0.71	-	-	-

Legend: Results from multivariable logit model with CRN as binary outcome and the numbers were weighted using 2004 HRS sample weight.

Table 3. Characteristics by age groups and deceased.

	Alive through the follow-up (N=9,896 for 50-79; 529 for 80+), representing 45,250,287; 1,856,348 after 2004 Weights	Deceased during follow-up (N=3,358 for 50-79, 2,137 for 80+), representing 12,271,988; 5,853,579 after 2004 Weights	P-value
Age group 50-79 in 2004			
Any CRN during the follow-up: %	27.15	21.20	<0.001
Average CRN during the follow-up: %/Year (s.d.)	9.20 (0.19)	10.8 (0.25)	<0.001
Age group 80+ in 2004			
Any CRN during the follow-up: %	12.39	8.63	<0.001
Average CRN during the follow-up: %/Year (s.d.)	3.1 (1.0)	4.6 (1.7)	<0.001

Legend: the numbers were weighted using 2004 HRS sample weight.

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3 Figure 1. Population-adjusted CRN Rates by Age Cohort 20004-2014
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5 Legend: the numbers were weighted using 2004 HRS sample weight.
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9 Figure 2. Trend in Ratio of Social Security Income to Total Income by Age Cohort 2004-2014.

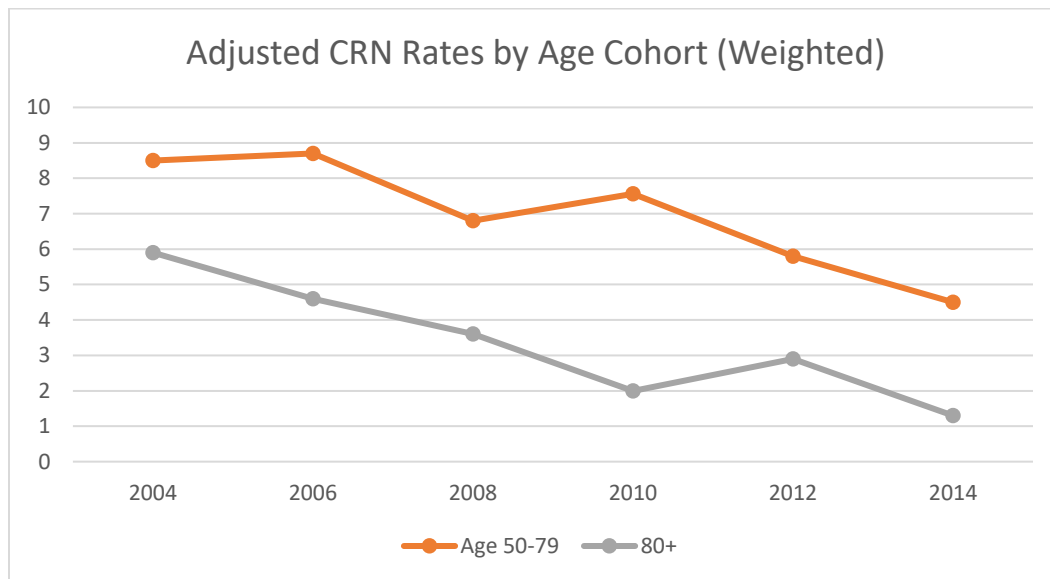
10 Legend: the numbers were weighted using 2004 HRS sample weight.
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14 Figure 3. Trend in Total Income Adjusted for Inflation by Age Cohort
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16 Legend: the numbers were weighted using 2004 HRS sample weight. The total income is adjusted using inflation
17 rates from the U.S. Department of Labor's Bureau Labor Statistics' Inflation Calculator.
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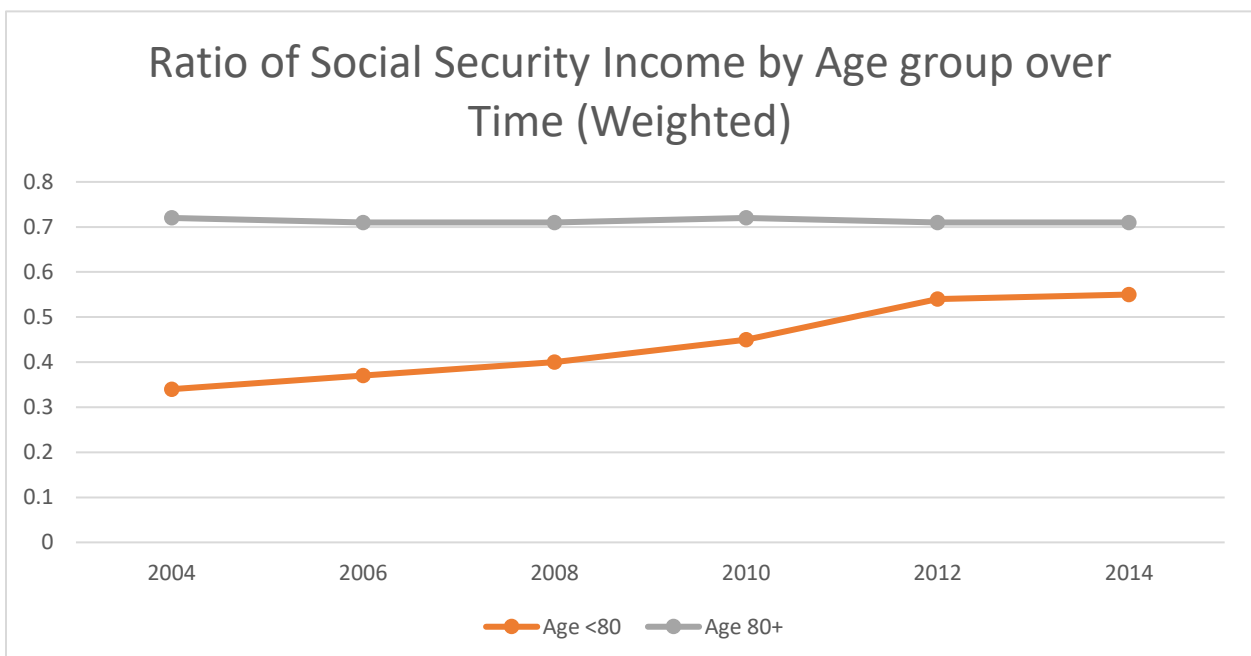
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21 **Appendix I. Source of Income**
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Figure 1. Population-adjusted CRN Rates by Age Cohort 2004-2014



Legend: the numbers were weighted using 2004 HRS sample weight.

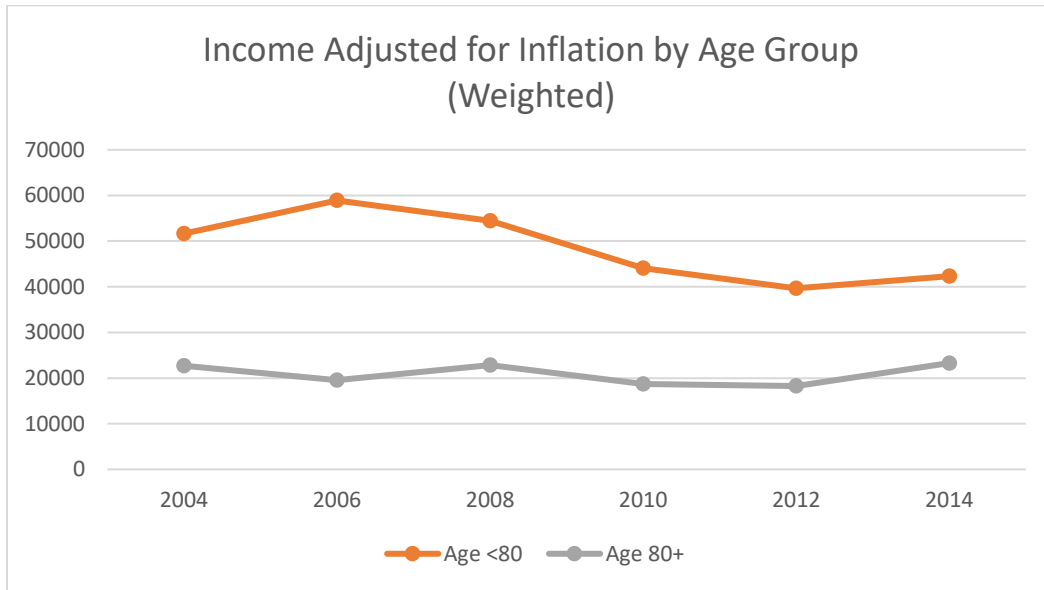
Figure 2. Trend in Ratio of Social Security Income to Total Income by Age Cohort 2004-2014.



Legend: the numbers were weighted using 2004 HRS sample weight.

Review only

Figure 3. Trend in Total Income Adjusted for Inflation by Age Cohort



Legend: the numbers were weighted using 2004 HRS sample weight. The total income is adjusted using inflation rates from the U.S. Department of Labor's Bureau Labor Statistics' Inflation Calculator.

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3 **Appendix I. Source of Income**
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Economic Variables
SOCIAL SECURITY INCOME
SUPPLEMENTAL SECURITY INCOME
AMOUNT FROM WORK SELF EMPL LCY
AMOUNT FROM WAGES AND SALARY LCY
AMOUNT FROM PROF PRAC OR TRADE LCY
AMOUNT FROM TIP BONUS COMMISSION LCY
AMOUNT FROM WORK 2ND JOB LCY
AMOUNT FROM UNEMPLOYMENT - LCY
AMOUNT FROM WORKERS COMP LCY
AMOUNT FROM WELFARE LCY
INC FROM OTHER IRA ANNUITY AMT
OTHER PENSIONS
OTHER ANNUITIES
STOCK INCOME AMOUNT - LCY
BOND INCOME AMOUNT - LCY
CDS INCOME AMOUNT - LCY
OTHER ASSET INCOME AMOUNT
OTHER SOURCES OF INCOME AMOUNT - LCY
VETERAN BENEFITS
AMOUNT RECEIVED FROM PENSION
AMOUNT FROM ANNUITY
AMOUNT FROM FOOD STAMPS

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

	Reporting Item	Page Number
Title and abstract		
Title	#1a Indicate the study's design with a commonly used term in the title or the abstract	1

1	Abstract	#1b	Provide in the abstract an informative and balanced summary	2
2			of what was done and what was found	
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6	Introduction			
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9				
10	Background /	#2	Explain the scientific background and rationale for the	4
11	rationale		investigation being reported	
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14				
15	Objectives	#3	State specific objectives, including any prespecified	5
16			hypotheses	
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20	Methods			
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22				
23	Study design	#4	Present key elements of study design early in the paper	5
24				
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26	Setting	#5	Describe the setting, locations, and relevant dates, including	6
27			periods of recruitment, exposure, follow-up, and data	
28			collection	
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34	Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of	6
35			selection of participants. Describe methods of follow-up.	
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39	Eligibility criteria	#6b	For matched studies, give matching criteria and number of	6
40			exposed and unexposed	
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45	Variables	#7	Clearly define all outcomes, exposures, predictors, potential	7
46			confounders, and effect modifiers. Give diagnostic criteria, if	
47			applicable	
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53	Data sources /	#8	For each variable of interest give sources of data and details	6
54	measurement		of methods of assessment (measurement). Describe	
55			comparability of assessment methods if there is more than	
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one group. Give information separately for for exposed and unexposed groups if applicable.

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6	Bias	#9	Describe any efforts to address potential sources of bias 7
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9	Study size	#10	Explain how the study size was arrived at 9
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12	Quantitative	#11	Explain how quantitative variables were handled in the 7
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14	variables		analyses. If applicable, describe which groupings were
15			chosen, and why
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19	Statistical	#12a	Describe all statistical methods, including those used to
20			control for confounding
21	methods		
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31	Statistical	#12b	Describe any methods used to examine subgroups and
32			interactions
33	methods		
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39	Statistical	#12c	Explain how missing data were addressed
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41	methods		
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45	Statistical	#12d	If applicable, explain how loss to follow-up was addressed
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47	methods		
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52	Statistical	#12e	Describe any sensitivity analyses N/A
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54	methods		
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1 **Results**

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- 4 Participants [#13a](#) Report numbers of individuals at each stage of study—eg
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- 6 numbers potentially eligible, examined for eligibility,
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- 8 confirmed eligible, included in the study, completing follow-
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- 10 up, and analysed. Give information separately for for
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- 12 exposed and unexposed groups if applicable. 9
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- 16 Participants [#13b](#) Give reasons for non-participation at each stage N/A
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- 19 Participants [#13c](#) Consider use of a flow diagram N/A
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- 26 Descriptive data [#14a](#) Give characteristics of study participants (eg demographic,
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- 28 clinical, social) and information on exposures and potential
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- 30 confounders. Give information separately for exposed and
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- 32 unexposed groups if applicable. 9
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- 36 Descriptive data [#14b](#) Indicate number of participants with missing data for each
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- 38 variable of interest 6
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- 44 Descriptive data [#14c](#) Summarise follow-up time (eg, average and total amount) 9
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- 50 Outcome data [#15](#) Report numbers of outcome events or summary measures
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- 52 over time. Give information separately for exposed and
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- 54 unexposed groups if applicable. 9
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1	Main results	#16a	Give unadjusted estimates and, if applicable, confounder-
2			adjusted estimates and their precision (eg, 95% confidence
3			interval). Make clear which confounders were adjusted for
4			and why they were included
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10	Main results	#16b	Report category boundaries when continuous variables were
11			categorized N/A
12	Main results	#16c	If relevant, consider translating estimates of relative risk into
13			absolute risk for a meaningful time period N/A
14			
15			
16	Other analyses	#17	Report other analyses done—eg analyses of subgroups and
17			interactions, and sensitivity analyses
18			10
19			
20	Discussion		
21			
22	Key results	#18	Summarise key results with reference to study objectives
23			11
24	Limitations	#19	Discuss limitations of the study, taking into account sources
25			of potential bias or imprecision. Discuss both direction and
26			magnitude of any potential bias.
27			13
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29	Interpretation	#20	Give a cautious overall interpretation considering objectives,
30			limitations, multiplicity of analyses, results from similar
31			studies, and other relevant evidence.
32			12
33	Generalisability	#21	Discuss the generalisability (external validity) of the study
34			results
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36	Other Information		
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1 Funding [#22](#) Give the source of funding and the role of the funders for the
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3 present study and, if applicable, for the original study on
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5 which the present article is based 14
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9 None The STROBE checklist is distributed under the terms of the Creative Commons Attribution
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BMJ Open

Decreasing Rates of Cost-Related Medication Non-Adherence by Age Advancement Among Old and Older-Old Americans: A Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-051480.R1
Article Type:	Original research
Date Submitted by the Author:	23-Sep-2021
Complete List of Authors:	Zhang, James; The University of Chicago, Medicine; 5841 S Maryland Ave. Bhaumik, Deepon Meltzer, David; The University of Chicago
Primary Subject Heading:	Health economics
Secondary Subject Heading:	Health economics, Health policy, Health services research
Keywords:	Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, EPIDEMIOLOGY, HEALTH ECONOMICS

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3 **Decreasing Rates of Cost-Related Medication Non-Adherence by Age Advancement Among Old**
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5 **and Older-Old Americans: A Longitudinal Study**
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33 Total number of words: 2,716

34 Running title: Aging and cost-related medication non-adherence

35
36 Key words: cost-related medication non-adherence, aging, paradox

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39 Total number of tables: 2

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41 Total number of Figures: 2
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45 ACKNOWLEDGEMENT

46
47 The study was presented in part at the International Health Economics World Congress, Basel,
48
49 Switzerland, July 16, 2019. This study is supported in part by Chicago Center for Diabetes
50
51 Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30DK092949), NIH
52
53 5R21AG053749 (Meltzer & Zhang), and NIH P30AG066619 (Meltzer & Zhang).
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Abstract

(300 words)

Objectives: The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. Cost-related medication non-adherence (CRN) is an important measure of medication non-adherence behaviors that aim to avoid costs. While there is a body of literature on the cross-sectional analysis of CRN internationally, longitudinal study of CRN behaviors for the aging population is rare.

Design: Longitudinal study using the Health and Retirement Study to evaluate self-reported CRN biennially.

Setting: General population of older Americans.

Participants: Two cohorts of Americans aged between 50 and 79 (old) and 80 or above (older-old) followed from 2004 to 2014.

Intervention: Observational with no intervention.

Primary and secondary outcome measures: Longitudinal CRN rates for two cohorts of Americans aged between 50 and 79 (old) and 80 or above (older-old) followed from 2004 to 2014. Population-averaged effects of a broad set of variables including socio-demographics, Social Security (SS) income to total income ratio, insurance status, functional status, and comorbid conditions on CRN were derived using Generalized Estimating Equation (GEE) by taking into account repeated measurements of CRN over time for the two cohorts, respectively.

Results: The two old and older-old cohorts with 13,254 and 9,856 respondents represented 57.5 million and 7.7 million people in 2004, respectively. Decreasing CRN was observed in both old and older-old cohorts despite their increasing limitations in functional status and disease burden as measured by comorbidities and their increasing or steady reliance on social security income as the primary source of income. Aging is associated with lower rates of CRN among both cohorts ($p < 0.01$, respectively), controlling for all other risk factors.

Conclusion: The paradox of lower CRN with higher disease burden and increasing reliance on social security income suggests populations' CRN behaviors change as Americans age, bearing implications to social policy.

Summary

Strength of the study:

- Nationally representative study sample
- Longitudinal follow-up of CRN which is rare in the literature
- Population-averaged effects of a broad set of variables on CRN using the Generalized Estimating Equation (GEE)
- Social Security Income/total income variable in addition to a rich set of insurance variables for risk adjustment

Weakness of the study

- Does not have information in change in the consumption bundle such as the other discretionary spending over time.

Introduction

The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. A recent national poll indicated that among those currently taking prescription drugs, one-fourth of adults (24 percent) and seniors (23 percent) have difficulty in affording their prescription drugs including about one in ten (overall and among seniors) saying it is “very difficult.”¹ Cost-related medication non-adherence (CRN) is a metric measuring such cost-avoiding behaviors and has seen an emerging body of literature on its prevalence internationally. For example, in a study of adults aged 55 and older and living in the community in 11 developed countries, the authors found that following the lead of the U.S. with 16.8% in CRN to medication, Canada had the second highest national prevalence of CRN (8.3%), followed by Australia (6.8%).² Many patients engage in strategies to avoid such costs when facing difficult choices between their medication needs and other basic needs, including delaying filling prescription, not filling prescriptions, skipping doses and splitting doses. Many behavioral, social, economic, medical, and policy-related factors have been identified as contributing factors for medication non-adherence.³⁻⁵ Medication non-adherence is associated with increased hospitalization rates and emergency department visits, higher mortality rates, worse patient outcomes, and increased downstream costs that impose heavy, avoidable healthcare costs on society.⁶⁻¹¹ Hence it is pressing for researchers, practitioners, and policy makers to gain insight into the key factors that drive the difference in CRN across population strata.

Among the many risk factors for CRN, age receives little attention even though younger disabled patients have been found to have higher CRN rates among the Medicare population.¹² In essence, age is a complex variable reflecting multiple dimensions of biological and social factors that can potentially drive-up CRN. For example, since older people may have protection from the

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3 Medicare insurance coverage including Part D outpatient prescription drug program, and at the
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5 same time, older people also have lower income and may suffer from multiple chronic conditions
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7 which require greater out-of-pocket spending on medications, and thus the tension between their
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9 resources and medication needs is relatively higher. The literature on the effect of aging process
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11 on CRN is scant, and most reported differences in CRN due to age is examined in the context of
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13 cross-sectional studies, which makes it unclear if the age difference in CRN is due to
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15 generational difference (i.e., cohort effect) or the aging process itself and also lacks of adequate
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17 control for the confounding factors. It is important to study the effects of the aging process on
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19 CRN because if the older people with less economic resource and higher disease burden reported
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21 lower CRN rates, *ceteris paribus*, it may mean they are actually cutting down spending on other
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23 basic needs and that therefore social policy may need to be revamped to address this hidden
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25 crisis. On the other hand, this is an interesting question about the behavioral change in the aging
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27 process, as it may reflect the change in the assessment of the value of medication (and life) as
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29 people progress to more advanced age.
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35 We hence propose to study the CRN behaviors among the older population in the US
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37 longitudinally. The longitudinal analysis isolates the cohort effect from its tempering of the age
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39 effect, and the broad set of controlling variables (particularly income and insurance variables)
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41 further isolate the potential confounding. We used the Health and Retirement Study (HRS), a
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43 nationally representative sample of older people (50 years or older), to generate population-
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45 averaged effects of age on CRN, controlling for a broad set of socio-demographic, insurance, and
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47 health variables.
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51 **Methods**

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Data

Data from HRS from 2004 to 2014 were used for this study. The HRS is a longitudinal panel study that surveys a representative sample of Americans over the age of 50 about their income, employment, health insurance, physical health, functional status, and medical conditions.¹³ Data for the survey is collected primarily by telephone interview every 2 years. Mortality was recorded if the respondent was deceased during the follow-up.

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. For those who refused to answer or say that they did not know, the answer is treated as no CRN was reported.

Cohort creation

We created two cohorts with age between 50 and 79 (old) and 80 or above (older-old) in 2004 and followed them to 2014 and evaluated CRN over time. The reason for creating two cohorts is to isolate the generational difference in CRN behaviors at baseline, and to compare the trajectory of CRN behaviors in these two cohorts by controlling other confounding factors. Such a grouping is also consistent with the older population defined by the US Census.¹⁴ The reason for the follow-up between 2004 and 2014 is that although the two cohorts experienced the Great Recession starting in 2008, the economy had largely recovered in steady growth by 2014 and hence this period of 10 years provides a clear picture of the trajectory of CRN pre-, during, and post-economic recession with up to six observations for each correspondent. The CRN rates were weighted to reflect the national estimates using 2004 survey weights.

Statistical analysis

Since our data included repeated measurement of CRN on a biannual basis for up to 6 measures, we developed a generalized estimating equation (GEE) to assess the population-averaged effect of a broad set of risk factors, including advancing age, on CRN, taking into account correlations among repeated observations of the patients, which are quite often unknown.¹⁵ One strength of such an approach is lower variability and thus more efficient comparison, allowing us to detect a difference within socio-economic strata in a sample with modest size within socio-economic strata. The GEE model uses a binomial family function, a probit link function, and an exchangeable correlation structure to address the binary outcome variable and correlation among the longitudinal follow-ups of the respondents. There is no particular order effect in the repeated measures in this analysis, as patients can report CRN intermittently, and the research has shown patients are not always persistent in CRN.¹⁶ In this analysis, the value of age variable increases by two years for each respondent for each round of surveys from 2004 to 2014. Our examination of the population-averaged effect of each risk factor on CRN gives us further evidence about the relationship between age and CRN while holding other variables constant, and the offsetting effects among those variables.

Covariates

These covariates included socio-demographics including gender, race, and ethnicity. Since insurance status has been found an important predictor for CRN,¹⁷ we included a set of indicator variables for those who were enrolled in Medicare, Medicaid, other types of public insurance, private insurance, and no insurance in each round of survey, which changed over time. Enrollment in Medicaid would indicate that they were at the lowest rung of the economic ladder, since Medicaid is a means-tested, state-sponsored public insurance program for those who meet

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3 the poverty level defined by each state. Research has also shown those with Medicare-Medicaid
4 dual eligibility (dual eligible) can have high CRN rates despite the additional insurance coverage,
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6 likely due to the fact that those at the bottom of the economic ladder are highly sensitive to the
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8 out-of-pocket payment or non-monetary reasons.¹⁸ Hence we included an indicator variable of
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10 Medicare-Medicaid dual eligibility in each round. The inclusion of Medicare, Medicaid
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12 coverage, Medicare-Medicaid dual eligibility and other insurance status variables will tease out
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14 the enabling effect of health insurance on overcoming resource limitation for the poor. Although
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16 not all respondents were eligible for Medicare, and a significant fraction of Medicare
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18 beneficiaries had creditable drug coverage and did not enroll in Medicare Part D outpatient
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20 prescription drug program,¹⁹ we included one additional indicator variable for Part D enrollment
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22 at each round between 2006 and 2014 to further control potential confounding.
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28 We also included two variables on functional status: limitations in Activities of Daily Living
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30 (ADLs), and Instrumental Activities of Daily Living (IADLs) in each round of surveys.^{20,21}
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32 These two variables measure the number of limitations in performing tasks such as dressing,
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34 bathing, eating, toileting, getting out of bed, and walking (ADLs), and preparing meals,
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36 shopping, managing money, and taking phone calls (IADLs). Research has also that functional
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38 status is an important factor influencing CRN.²² We also included a set of comorbid conditions
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40 including diabetes, heart disease, stroke, and cancer in each round of surveys. These conditions
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42 are known to have high disease burden for patients in terms of both the need for continuous
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44 medical care and high costs of medication treatments.¹⁷
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49 In addition, we created a variable for the ratio of social security (SS) to total income in each
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51 round of surveys in order to further isolate the effect of income on CRN from potential
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53 confounding. HRS has a rich set of questionnaires on sources of income and given that many of
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3 the elderly are already in retirement and wage income would have been a poor proxy, we first
4 created one variable for total income, including wages, pensions, unemployment benefits, SS
5 income, and income from investments and financial assets for each patient. (See Appendix I for a
6 list of sources of income). Because not every income-related variable is measured on a monthly
7 basis, we extrapolated these variables to its annual amount. We then created a variable indicating
8 the ratio of SS income to total income. Because not all respondents reported income, we created
9 one dummy variable indicating those who did not report income. We set the SSI/Income variable
10 to zero if income information is missing in its entirety or zero income was reported in the
11 regression as SSI were unknown or zero. We think that SS-income ratio reflects the degree to
12 which the respondent relies on SS income for their daily lives in relative terms. Research showed
13 that in 2013, Medicare beneficiaries' average out-of-pocket health care spending was 41 percent
14 of average per capita SS income,²³ suggesting the importance of using SS income as a
15 benchmark for resource availability for the elderly at the population level. The higher SS-income
16 ratio would indicate smaller room for trade-off between the medication needs and other daily
17 needs as the respondents have no other economic resources to turn to once they use up the SS
18 income, which is often too low to sustain a life given all of their disease burdens.

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20 We compared the demographic variables, insurance status, and comorbid conditions for each
21 cohort at 2004 and 2014 respectively, using Chi-squared tests. We compared the number of
22 functional status between 2004 and 2014 for the two cohorts using t-tests. All analyses were
23 weighted to reflect the population average. The analyses were conducted using Stata Version 14
24 (StataCorp, College Station, Texas 77845, USA).

25 *Patient and Public Involvement*

26 No patient involved.

Results

Table 1 shows the demographics, SSI/total income ratio, insurance status, functional status, and comorbid conditions at the baseline of 2004 and at the end of follow-up of 2014, for the two old and older-old cohorts, with 13,254 and 9,856 respondents representing 57.5 million and 7.7 million people at the baseline, respectively. All respondents 50 years or old in the HRS were included. After 10 years, 9,856 and 529 patients remained alive in the two cohorts representing 45.2 million and 1.82 million people at 2014 after ascertaining death recorded in the HRS. The observed CRN prevalence rates were 10.4% and 4.6% at 2004, and decreased to 7.31% and 2.06% in 2014, for the old and older-old cohorts, ($p<0.01$, respectively). There were significant changes in patient mix in both cohorts over time. Overall, the functional limitations in both ADLs and IADLs, and the prevalence of comorbid conditions by four conditions increased in both cohorts ($P<0.01$, respectively).

Table 2 shows the population-averaged estimates of age effect along with other risk factors for the old and older-old cohorts, respectively. Aging is associated with lower rates of CRN among both cohorts ($p<0.01$, respectively), controlling for all other risk factors. In both cohorts, females were more likely to report CRN than males ($p<0.01$, $p=0.04$, respectively). While insurance status, comorbid conditions, and functional status had significant impact on CRN in the old cohort, such impact became statistically insignificant in the older-old cohort.

Figure 1 shows the observed CRN rates by age cohort from 2004 to 2014. There was a general downward trend in both age cohort, despite a small bump between 2008 and 2012 when the economy was in turmoil due to the Great Recession. Figure 2 shows the observed SSI/Income ratio by age cohort from 2002 to 2014. There was a general upward trend in the old age cohort, while the ratio held largely steady among the older-old cohort.

Discussion and Conclusions

There was a clear downward trend in the CRN prevalence rates in both old and older-old cohorts between 2004 and 2014, despite economic downturn after 2008 due to the Great Recession. After controlling for other risk factors including gender, race, ethnicity, various insurance status, comorbid conditions, and functional status, aging was significantly negatively associated with CRN as people age.

Such a steady decrease in CRN rates was accompanied by increasing limitations in functional status in both ADLs and IADLs and increasing prevalence of comorbid conditions, reflecting heightened frailty and disease burden in both cohorts as they aged. There was an increase in the Medicaid enrollment in both cohorts, which likely provides protection from CRN. However, even after adjusting for Medicaid and all other insurance variables, the clear pattern of decreasing CRN is still seen as the population ages.

This “paradox” of decreasing CRN rates among old Americans as they age, who rely increasingly on social security income and bear a higher disease burden, which requires a higher consumption of medications, seems to be robust, persisting through a series of controls for confounding factors. One possible explanation is that as the population ages and faces a shorter remaining life-span, the value of medication may change, resulting in the population changing their consumption bundle and devoting more resources to medication use. Because the elderly population is increasingly dependent on their fixed SS income, such a change in their consumption bundle will inevitably decrease their ability to afford other daily needs, such as housing, food, and transportation. There is little literature in this aspect of the loss of welfare due to the pressure to pay for the medications. More research is greatly needed to evaluate the adequacy of social policy to help the elderly cope with increasing demand for medications as

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3 they age. When CRN was examined longitudinally, one recent study suggested that younger age
4 is a risk factor for persistent CRN.¹⁶ The evidence from this study corroborates that patient's
5 behavior may evolve when they age.
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10 This study is limited by the fact that the HRS does not have data to examine the subjective
11 evaluation of consumption bundles in order to derive the exact cause of decreasing CRN despite
12 increasing disease burden and decreasing economic resources. Nor does the HRS allows an
13 exhaustive examination of consumption by goods and services. Future research should be
14 directed to examine these issues and to further illuminate the changing consumption preferences
15 of the elderly. Needless to say, such a change is forced upon them when the elderly is faced with
16 decreasing economic resources at the same time as higher disease burdens. Further
17 understanding of the coping mechanisms and trade-offs faced by the elderly may have profound
18 implications for social policy that aims to protect the elderly.
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30 *Conclusion*

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33 In summary, we presented a clear case of decreasing CRN rates among the old and older-old
34 cohorts despite decreasing economic resources, increasing disease burden, and increasing
35 Medicaid coverage. Such a paradox is possibly driven by the change in preferences for
36 medication or the perceived value of medications as the population ages. This may suggest a
37 hidden gap in social policy as the elderly cope with increased burdens by reducing consumption
38 of other goods and services which may reduce their overall well-being. More research is greatly
39 needed to understand this phenomenon and improve social policy for our aging population.
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ACKNOWLEDGEMENT

The study was presented in part at the International Health Economics World Congress, Basel, Switzerland, July 16, 2019. We are indebted to the constructive comments by the reviewer.

FUNDING STATEMENT

This study is supported in part by Chicago Center for Diabetes Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30 DK092949), NIH 5R21AG053749 (Meltzer & Zhang), and NIH P30AG066619 (Meltzer & Zhang). The funders have no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

AUTHOR CONTRIBUTIONS

Dr Zhang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Zhang.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Zhang.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Bhaumik, Zhang.

Obtained funding: Meltzer, Zhang.

Administrative, technical, or material support: Meltzer, Zhang.

Supervision: Zhang.

COMPETING INTEREST STATEMENT

Dr. Meltzer reported receiving compensation from CVS Consultant outside the submitted work. No other disclosures were reported.

ETHICAL APPROVAL

The public use file of the Health and Retirement Study does not have human subjects, hence patient consent or the approval by the Institutional Review Board is not required.

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DATA SHARING STATEMENT

The public use file of the Health and Retirement Study can be downloaded directly from its webpage accessible at <https://hrs.isr.umich.edu/about>.

For peer review only

REFERENCES

1. Kaiser Family Foundation. KFF Health Tracking Poll – February 2019: Prescription Drugs. 2019. Available <https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/>. Accessed August 14, 2020.
2. Morgan SG, Lee A. Cost-related non-adherence to prescribed medicines among older adults: a cross-sectional analysis of a survey in 11 developed countries. *BMJ Open* 2017;7:e014287.
3. Gellad WF, Grenard J, McGlynn EA. A review of barriers to medication adherence: a framework for driving policy options. RAND Corporation, 2009. Available at: http://www.rand.org/pubs/technical_reports/TR765.html. Accessed March 1, 2019.
4. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004; 42:200-9.
5. National Council on Patient Information and Education. Enhancing Prescription Medicine Adherence: A National Action Plan. 2007. Available at http://www.talkaboutrx.org/documents/enhancing_prescription_medicine_adherence.pdf. Accessed February 4, 2017.
6. Tamblyn R, Laprise R, Hanley JA, Abrahamowicz M, Scott S, Mayo N, Hurley J, Grad R, Latimer E, Perreault R, McLeod P, Huang A, Larochelle P, Mallet L Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001; 285:421–429.
7. Mojtabei R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff*. 2003; 22(4):220–229.
8. Heisler M, Langa KM, Eby EL, Fendrick AM, Kabeto MU, Piette JD. The health effects of restricting prescription medication use because of cost. *Med Care*. 2004; 42:626–634.
9. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006; 166:1836–1841.
10. Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ, Krumholz HM, Rumsfeld JS. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Arch Intern Med*. 2006; 166:1842–1847.
11. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014 Feb 20; 7:35-44.
12. Soumerai SB, Pierre-Jacques M, Zhang F, et al. Cost-related medication nonadherence among elderly and disabled Medicare beneficiaries: a national survey 1 year before the medicare drug benefit. *Arch Intern Med*. 2006;166(17):1829-1835.
13. The Health and Retirement Study. Available <https://hrs.isr.umich.edu/about>. Accessed August 20, 2020.
14. The US Census. The Older Population in the United States: 2004. Available <https://www.census.gov/data/tables/2004/demo/age-and-sex/2004-older-population.html>. Accessed August 24, 2020.
15. Liang KY and Zeger S. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 73 (1): 13–22.

16. De Avila JL, Meltzer DO, Zhang JX. Prevalence and Persistence of Cost-Related Medication Nonadherence Among Medicare Beneficiaries at High Risk of Hospitalization. *JAMA Netw Open*. 2021;4(3):e210498. doi:10.1001/jamanetworkopen.2021.0498
17. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med*. 2007;22(6):864-71.
18. Zhang JX, Meltzer DO. The High Cost-related Medication Non-adherence Rate Among Medicare-Medicaid Dual-Eligible Diabetes Patients. *J Health Med Econ*. 2016;2(2).
19. Kaiser Family Foundation. An Overview of the Medicare Part D Prescription Drug Benefit. Available at <https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/>. Accessed September 22, 2021.
20. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. the index of adl: a standardized measure of biological and psychosocial function. *Journal of American Medical Association*. 1963; 185:914-919.
21. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179-186.
22. Zhang JX, Meltzer DO. Risk factors for cost-related medication non-adherence among older patients with cancer. *Integr Cancer Sci Ther*. 2015;2(6):300-304.
23. Kaiser Family Foundation. Medicare Beneficiaries' Out-of-Pocket Health Care Spending as a Share of Income Now and Projections for the Future. 2018. Available <https://www.kff.org/medicare/report/medicare-beneficiaries-out-of-pocket-health-care-spending-as-a-share-of-income-now-and-projections-for-the-future/>. Accessed August 24, 2020.

Table 1. Socio-economic and health characteristics of the study sample.

	Age 50-79 in 2004		P-value	Age ≥ 80 in 2004		P-value
	2004	2014		2004	2014	
Total N: sample (weighted)	13,254 (57,522,395)	9,856 (45,250,407)		2,666 (7,709,927)	529 (1,856,348)	
CRN (% of total)	10.42	7.31	<0.01	4.64	2.06	<0.01
<i>Demographics</i>						
Mean Age (SD)	62.3 (8.2)	70.9 (7.7)	<0.01	84.6 (3.9)	92.8 (2.6)	<0.01
Male N (%)	26,537,035 (46.13)	19,959,531 (44.11)	<0.01	2,865,953 (37.17)	549,748 (29.61)	<0.01
<i>Race</i>						
White N (%)	46,566,916 (81.0)	36,778,482 (81.3)	<0.01	6,722,307 (87.2)	1,648,583 (88.8)	<0.01
Black N (%)	5,422,810 (9.4)	3,946,334 (8.7)	<0.01	563,630 (7.3)	123,727 (6.7)	<0.01
Other N (%)	1,533,962 (2.7)	1,299,172 (2.9)	<0.01	82,439 (1.1)	13,734 (0.7)	<0.01
Hispanic N (%)	1,498,296 (7.0)	3,218,998 (7.1)	<0.01	341,551 (4.4)	70,304 (3.79)	<0.01
High School Degree N (%)	44,792,359 (78.1)	36,771,098 (81.6)	<0.01	5,104,259 (66.2)	1,382,472 (74.5)	<0.01
<i>Income</i>						
Did not report income N(%)	23,628,988 (41.08)	29,017,063 (50.44)	<0.01	1,700,631 (22.06)	6,366,197 (82.57)	<0.01
Mean Social Security to Income Ratio (SD)	0.34 (0.40)	0.56 (0.40)	<0.01	0.72 (0.32)	0.72 (0.33)	<0.10
<i>Health Insurance status</i>						
Medicare N (%)	23,977,429 (41.73)	33,886,106 (75.22)	<0.01	7,551,255 (98.27)	1,783,088 (96.82)	<0.01
Medicaid Only N (%)	4,347,512 (7.57)	4,195,261 (9.34)	<0.01	741,106 (9.68)	376,197 (20.77)	<0.01
Dual Eligible N (%)	2,782,874 (4.85)	3,546,866 (7.90)	<0.01	697,373 (9.11)	345,825 (19.09)	<0.01
Private Insurance N (%)	41,518,125 (72.28)	24,488,109 (54.58)	<0.01	5,025,727 (65.64)	797,828 (44.76)	<0.01
Other Public Insurance N (%)	2,972,999 (5.17)	3,075,241 (6.82)	<0.01	387,785 (5.05)	118,750 (6.44)	<0.01
No Insurance N (%)	3,861,461 (6.71)	1,196,071 (2.08)	<0.01	14,157 (0.18)	17,155 (0.22)	<0.01
Medicare Part D	0 (0)	11,189,901 (24.73)	-	0 (0)	661,142 (35.62)	-
<i>Functional status</i>						
Activities of Daily Life N (SD) (dress, bath, walk, eat, bed, toilet)	1.11 (1.93)	1.20 (1.97)	<0.01	1.36 (1.94)	2.19 (2.27)	<0.01
Instrumental Activities of Daily Life N (SD)	0.24 (0.65)	0.35 (0.86)	<0.01	0.85 (1.24)	1.82 (1.65)	<0.01

(meal, shop, phone, money)						
<i>Comorbid condition</i>						
Cancer N (%)	6,729,897 (11.8)	8,279,802 (18.5)	<0.01	1,601,000 (21.1)	463,700 (25.4)	<0.01
Diabetes N (%)	9,870,732 (17.3)	11,607,147 (25.9)	<0.01	1,268,614 (16.8)	387,277 (21.2)	<0.01
Heart Condition N (%)	11,463,265 (20.07)	12,694,226 (28.3)	<0.01	3,141,721 (41.5)	897,113 (49.21)	<0.01
Stroke N (%)	2,981,224 (5.2)	3,558,686 (7.94)	<0.01	972,042 (12.8)	392,876 (21.6)	<0.01

Legend: the numbers were weighted using 2004 HRS sample weight except the first row representing the sample.

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Table 2. Association between Age, Other Risk Factors and CRN from Generalized Estimating Equation for Old, and Older-old cohorts from 2004 to 2014.

	Old cohort (aged 50-79 in 2004)				Old cohort (aged 80+ in 2004)			
	Coef.	P>z	95% CI Lower bound	95% CI Upper bound	Coef.	P>z	95% CI Lower bound	95% CI Upper bound
Age	-0.03	<0.01	-0.03	-0.03	-0.03	<0.01	-0.05	-0.01
Female	0.31	<0.01	0.26	0.36	0.15	0.04	0.01	0.30
White	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Black	0.21	<0.01	0.14	0.27	0.41	<0.01	0.20	0.62
Other Race	0.08	0.33	-0.08	0.23	-0.51	0.21	-1.31	0.29
Hispanic	0.02	0.60	-0.06	0.10	0.18	0.16	-0.07	0.44
SSI/income Ratio	0.10	<0.01	0.04	0.16	0.14	0.12	-0.03	0.31
Not reporting income	-0.09	<0.01	-0.14	-0.03	-0.08	0.34	-0.26	0.09
High School	-0.23	<0.01	-0.29	-0.17	-0.05	0.54	-0.20	0.11
Medicare	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Medicaid	-0.10	0.13	-0.22	0.03	0.35	0.12	-0.10	0.80
Dual eligibility	-0.06	0.41	-0.19	0.08	-0.41	0.09	-0.88	0.06
Uninsured	0.30	<0.01	0.21	0.38	0.12	0.76	-0.65	0.89
Private Insurance	-0.20	<0.01	-0.25	-0.15	-0.11	0.12	-0.24	0.03
Other Public Insurance	-0.29	<0.01	-0.40	-0.19	-0.30	0.11	-0.66	0.07
Part D	0.13	<0.01	0.08	0.18	<0.01	0.97	-0.13	0.13
Diabetes	0.27	<0.01	0.22	0.32	0.01	0.92	-0.20	0.22
Cancer	0.01	0.72	-0.05	0.07	-0.04	0.60	-0.21	0.12
Heart	0.22	<0.01	0.17	0.27	0.11	0.12	-0.03	0.24
Stroke	0.06	0.15	-0.02	0.15	0.13	0.15	-0.05	0.32
ADL Deficiency	0.01	0.03	<0.01	0.02	0.01	0.45	-0.02	0.04
IADL Deficiency	0.07	<0.01	0.05	0.10	0.02	0.60	-0.04	0.07

Legend: Results from Generalized Estimating Equation with CRN as binary outcome and weighted using 2004 HRS sample weight ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.

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5 Figure 1. Observed CRN Rates by Age Cohort 2004-2014
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7 Legend: the numbers were weighted using 2004 HRS sample weight.
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11 Figure 2. Trend in Ratio of Social Security Income to Total Income by Age Cohort 2004-2014.
12

13 Legend: the numbers were weighted using 2004 HRS sample weight. Data included those who
14 reported non-zero total income only.
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16

17 **Appendix I. Source of Income**
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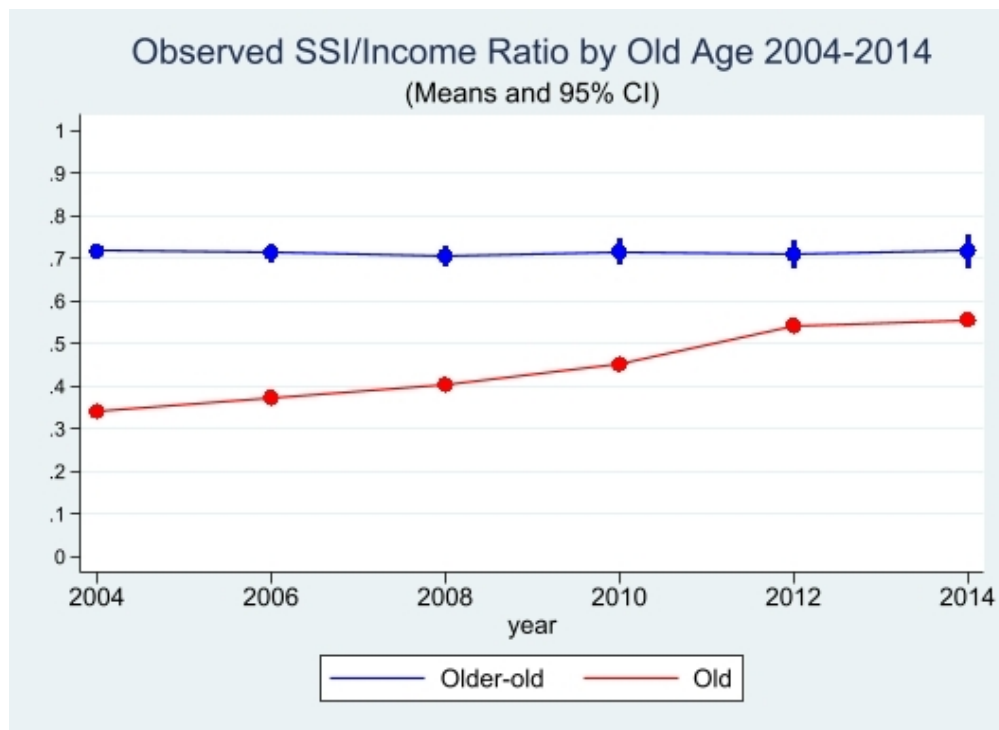


Figure 1. Observed CRN Rates by Age Cohort 2004-2014

Legend: the numbers were weighted using 2004 HRS sample weight.

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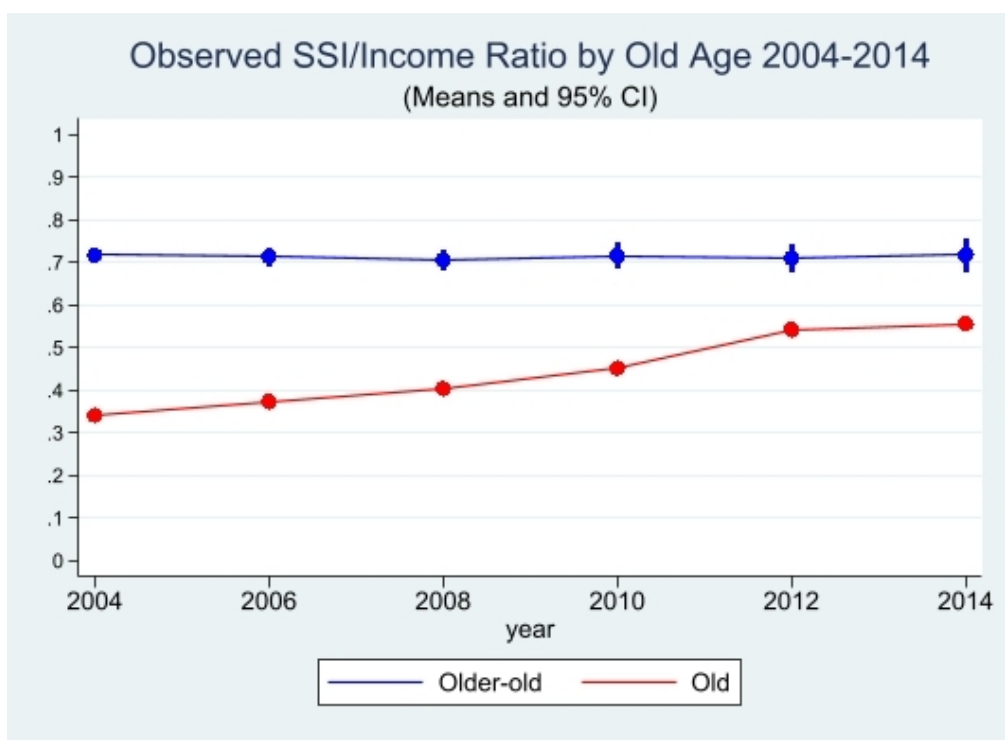


Figure 2. Trend in Ratio of Social Security Income to Total Income by Age Cohort 2004-2014.

Legend: the numbers were weighted using 2004 HRS sample weight. Data included those who reported non-zero total income only

139x101mm (96 x 96 DPI)

1
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3 **Appendix I. Source of Income**
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Economic Variables
SOCIAL SECURITY INCOME
SUPPLEMENTAL SECURITY INCOME
AMOUNT FROM WORK SELF EMPL LCY
AMOUNT FROM WAGES AND SALARY LCY
AMOUNT FROM PROF PRAC OR TRADE LCY
AMOUNT FROM TIP BONUS COMMISSION LCY
AMOUNT FROM WORK 2ND JOB LCY
AMOUNT FROM UNEMPLOYMENT - LCY
AMOUNT FROM WORKERS COMP LCY
AMOUNT FROM WELFARE LCY
INC FROM OTHER IRA ANNUITY AMT
OTHER PENSIONS
OTHER ANNUITIES
STOCK INCOME AMOUNT - LCY
BOND INCOME AMOUNT - LCY
CDS INCOME AMOUNT - LCY
OTHER ASSET INCOME AMOUNT
OTHER SOURCES OF INCOME AMOUNT - LCY
VETERAN BENEFITS
AMOUNT RECEIVED FROM PENSION
AMOUNT FROM ANNUITY
AMOUNT FROM FOOD STAMPS

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Page
	Reporting Item	Number
Title and abstract		
Title	#1a Indicate the study's design with a commonly used term in the title or the abstract	1

1	Abstract	#1b	Provide in the abstract an informative and balanced summary	2
2			of what was done and what was found	
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5				
6	Introduction			
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8				
9				
10	Background /	#2	Explain the scientific background and rationale for the	4
11	rationale		investigation being reported	
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15	Objectives	#3	State specific objectives, including any prespecified	5
16			hypotheses	
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20	Methods			
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23	Study design	#4	Present key elements of study design early in the paper	5
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26	Setting	#5	Describe the setting, locations, and relevant dates, including	6
27			periods of recruitment, exposure, follow-up, and data	
28			collection	
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34	Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of	6
35			selection of participants. Describe methods of follow-up.	
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39	Eligibility criteria	#6b	For matched studies, give matching criteria and number of	6
40			exposed and unexposed	
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45	Variables	#7	Clearly define all outcomes, exposures, predictors, potential	7
46			confounders, and effect modifiers. Give diagnostic criteria, if	
47			applicable	
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53	Data sources /	#8	For each variable of interest give sources of data and details	7,8,9
54	measurement		of methods of assessment (measurement). Describe	
55			comparability of assessment methods if there is more than	
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one group. Give information separately for for exposed and unexposed groups if applicable.

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6	Bias	#9	Describe any efforts to address potential sources of bias 7
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9	Study size	#10	Explain how the study size was arrived at 10
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12	Quantitative	#11	Explain how quantitative variables were handled in the 7,8,9
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14	variables		analyses. If applicable, describe which groupings were
15			chosen, and why
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19	Statistical	#12a	Describe all statistical methods, including those used to
20			control for confounding
21	methods		
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31	Statistical	#12b	Describe any methods used to examine subgroups and
32			interactions
33	methods		
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39	Statistical	#12c	Explain how missing data were addressed
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46	Statistical	#12d	If applicable, explain how loss to follow-up was addressed
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48	methods		
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52	Statistical	#12e	Describe any sensitivity analyses N/A
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Results

- Participants [#13a](#) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for exposed and unexposed groups if applicable. 9
- Participants [#13b](#) Give reasons for non-participation at each stage N/A
- Participants [#13c](#) Consider use of a flow diagram N/A
- Descriptive data [#14a](#) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable. 9
- Descriptive data [#14b](#) Indicate number of participants with missing data for each variable of interest 9, 16
- Descriptive data [#14c](#) Summarise follow-up time (eg, average and total amount) 7
- Outcome data [#15](#) Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable. 10, 16

- 1 Main results [#16a](#) Give unadjusted estimates and, if applicable, confounder-
 2 adjusted estimates and their precision (eg, 95% confidence
 3 interval). Make clear which confounders were adjusted for
 4 and why they were included 10, 16, 17, 18
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 11 Main results [#16b](#) Report category boundaries when continuous variables were
 12 categorized N/A
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 16 Main results [#16c](#) If relevant, consider translating estimates of relative risk into
 17 absolute risk for a meaningful time period N/A
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 25 Other analyses [#17](#) Report other analyses done—eg analyses of subgroups and
 26 interactions, and sensitivity analyses 10
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 30 **Discussion**
 31
 32
 33 Key results [#18](#) Summarise key results with reference to study objectives 11
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 35
 36 Limitations [#19](#) Discuss limitations of the study, taking into account sources
 37 of potential bias or imprecision. Discuss both direction and
 38 magnitude of any potential bias. 12
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 44 Interpretation [#20](#) Give a cautious overall interpretation considering objectives,
 45 limitations, multiplicity of analyses, results from similar
 46 studies, and other relevant evidence. 11
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 52 Generalisability [#21](#) Discuss the generalisability (external validity) of the study
 53 results 12
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 57 **Other Information**
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1 Funding [#22](#) Give the source of funding and the role of the funders for the
2
3 present study and, if applicable, for the original study on
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5 which the present article is based 13
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BMJ Open

Decreasing Rates of Cost-Related Medication Non-Adherence by Age Advancement among American Generational Cohorts 2004-2014: A Longitudinal Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-051480.R2
Article Type:	Original research
Date Submitted by the Author:	28-Feb-2022
Complete List of Authors:	Zhang, James; The University of Chicago, Medicine; 5841 S Maryland Ave. Bhaumik, Deepon; Yale University Meltzer, David; The University of Chicago
Primary Subject Heading:	Health economics
Secondary Subject Heading:	Health economics, Health policy, Health services research
Keywords:	Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, EPIDEMIOLOGY, HEALTH ECONOMICS

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3 **Decreasing Rates of Cost-Related Medication Non-Adherence by Age Advancement among**
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5 **American Generational Cohorts 2004-2014: A Longitudinal Study**
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30
31 Total number of words: 2,923

32
33 Running title: Aging and cost-related medication non-adherence

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35 Key words: cost-related medication non-adherence, aging, paradox

36
37 Total number of tables: 2

38
39 Total number of Figures: 2
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42

43 ACKNOWLEDGEMENT

44
45 The study was presented in part at the International Health Economics World Congress, Basel,
46
47 Switzerland, July 16, 2019. This study is supported in part by Chicago Center for Diabetes
48
49 Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30DK092949), NIH
50
51 5R21AG053749 (Meltzer & Zhang), and NIH P30AG066619 (Meltzer & Zhang).
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Abstract

(298 words)

Objectives: The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. Cost-related medication non-adherence (CRN) is an important measure of medication non-adherence behaviors that aim to avoid costs. Longitudinal study of CRN behaviors for the aging population is rare.

Design: Longitudinal study using the Health and Retirement Study to evaluate self-reported CRN biennially.

Setting: General population of older Americans.

Participants: Three cohorts of Americans aged between 50 and 54 (baby boomers), 65-69 (the silent generation), and 80 or above (the greatest generation) in 2004 who were followed to 2014.

Intervention: Observational with no intervention.

Primary and secondary outcome measures: Longitudinal CRN rates for three generational cohorts from 2004 to 2014. Population-averaged effects of a broad set of variables including socio-demographics, income, insurance status, limitations in activities of daily living (ADLs) and instrumental activities of daily living (IADLs), and comorbid conditions on CRN were derived using Generalized Estimating Equation (GEE) by taking into account repeated measurements of CRN over time for the three cohorts, respectively.

Results: The three cohorts of baby boomer, the silent generation, and the greatest generation with 1,925, 2,839 and 2,666 respondents represented 12.3 million, 8.2 million and 7.7 million people in 2004, respectively. Increasing age was associated with decreasing likelihood of reporting CRN in all three generational cohorts ($p < 0.05$), controlling for demographics, income, insurance status, functional status, and comorbid conditions. All three generational cohorts had a higher prevalence of diabetes, cancer, heart conditions, stroke, a higher percentage of respondents with Medicare-Medicaid dual eligibility and lower percentage with private insurance in 2014 compared to 2004 ($p < 0.05$).

Conclusion: The paradox of decreasing CRN rates, independent of disease burden, income, and insurance status, suggests populations' CRN behaviors change as Americans age, bearing implications to social policy.

Summary

Strengths of the study:

- Nationally representative study sample
- Longitudinal follow-up of CRN (rare in the literature)
- Population-averaged effects of a broad set of variables on CRN using the Generalized Estimating Equation (GEE)
- A rich set of income, insurance status, and disease and functional status variables for risk adjustment

Weakness of the study

- Does not have information on change in consumption bundle, such as other discretionary spending over time.

Introduction

The access barrier to medication has been a persistent and elusive challenge in the US health care system and around the globe. A recent national poll indicated that among those currently taking prescription drugs, one-fourth of adults (24 percent) and seniors (23 percent) have difficulty in affording their prescription drugs including about one in ten (overall and among seniors) saying it is “very difficult.”¹ Cost-related medication non-adherence (CRN) measures cost-avoiding behaviors and has seen an emerging body of literature on its prevalence internationally. For example, in a study of adults aged 55 and older living in the community in 11 developed countries, the authors found that the U.S. had a CRN rate of 16.8%, Canada had the second highest national prevalence of CRN at 8.3%, and Australia followed at 6.8%.² Many patients engage in strategies to avoid such costs when facing difficult choices between their medication needs and other basic needs, including delaying filling prescriptions, not filling prescriptions, skipping doses, and splitting doses. Many behavioral, social, economic, medical, and policy-related factors have been identified as contributing to medication non-adherence.³⁻⁵ Medication non-adherence is associated with increased hospitalization rates and emergency department visits, higher mortality rates, worse patient outcomes, and increased downstream costs that impose heavy, avoidable healthcare costs on society.⁶⁻¹¹ Hence it is pressing for researchers, practitioners, and policy makers to gain insight into the key factors that drive the difference in CRN across population strata.

Among the many risk factors for CRN, age receives little attention even though younger disabled patients have been found to have higher CRN rates among the Medicare population.¹² Age is a complex variable, reflecting multiple dimensions of biological and social factors that can potentially drive up CRN. For example, while older people may have protection from Medicare insurance coverage, including the Part D outpatient prescription drug program, at the

1
2
3 same time they also have lower income and may suffer from multiple chronic conditions that
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5 require greater out-of-pocket spending on medications. Thus the tension between their resources
6
7 and medication needs is comparatively higher. The literature on the effect of the aging process
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9 on CRN is scant, and most reported differences in CRN due to age are examined in the context
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11 of cross-sectional studies. These studies make it unclear if the age difference in CRN is due to
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13 generational difference (i.e., cohort effect) or the aging process itself and also lack adequate
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15 control for the confounding factors. It is important to study the effects of the aging process on
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17 CRN because if older people with fewer economic resources and higher disease burdens report
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19 lower CRN rates, *ceteris paribus*, it may mean they are actually cutting down spending on other
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21 basic needs and that therefore social policy may need to be revamped to address this hidden
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23 crisis. On the other hand, this is an interesting question about the behavioral change in the aging
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25 process, as it may reflect the change in the assessment of the value of medication (and life) as
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27 people progress to more advanced age.
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33 We therefore propose to test the hypothesis of changing CRN rates among the older
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35 population in the US longitudinally. The longitudinal analysis isolates the cohort effect from its
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37 tempering of the age effect, and the broad set of controlling variables (particularly income and
38
39 insurance variables) further isolate the potential confounding. We used the Health and
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41 Retirement Study (HRS),¹³ a nationally representative sample of older people (50 years or older),
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43 to generate population-averaged effects of age on CRN, controlling for a broad set of socio-
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45 demographic, insurance, and health variables.
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49 **Methods**

50 *Data*

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3 Data from HRS from 2004 to 2014 were used for this study. The HRS is a longitudinal
4 panel study that surveys a representative sample of Americans over the age of 50 about their
5 income, employment, health insurance, physical health, functional status, and medical
6 conditions.¹³ Data for the survey is collected primarily by telephone interview every 2 years.
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8 Mortality was recorded if the respondent was deceased during the follow-up.
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14 CRN was measured by asking participants, “Sometimes people delay taking medication or
15 filling prescriptions because of the cost. At any time since the last interview or in the last two
16 years have you ended up taking less medication than was prescribed for you because of the
17 cost?” Participants answered either yes or no, although they had the option to refuse to answer or
18 say that they did not know. For those who refused to answer or say that they did not know, the
19 answer is treated as no CRN was reported.
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28 *Cohort creation*

29 We created three generational cohorts of Americans aged between 50 and 54 (baby boomer),
30 65-69 (the silent generation), and 80 or above (the greatest generation) in 2004, followed them to
31 2014, and evaluated CRN over time. The reason for creating these three cohorts is to isolate the
32 generational difference in CRN behaviors at baseline, and to compare the trajectory of CRN
33 behaviors in these three cohorts by controlling for other confounding factors. Such a grouping is
34 also consistent with the older population defined by the US Census and policy analysis.^{14,15} The
35 narrower band for cohort age further reduces boundary errors among the generations. The reason
36 for the follow-up between 2004 and 2014 is that although the three cohorts experienced the Great
37 Recession starting in 2008, the economy had largely recovered in steady growth by 2014 and
38 hence this period of 10 years provides a clear picture of the trajectory of CRN pre-, during, and
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3 post-economic recession with up to six observations for each correspondent. CRN rates were
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5 weighted to reflect the national estimates using 2004 survey weights.
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7 8 *Statistical analysis*

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10 Since our data included repeated measurement of CRN on a biannual basis for up to 6
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12 measures, we developed a generalized estimating equation (GEE) to assess the population-
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14 averaged effect of a broad set of risk factors, including advancing age, on CRN, taking into
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16 account correlations among repeated observations of the patients, which are quite often
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18 unknown.¹⁶ One strength of such an approach is lower variability and thus more efficient
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20 comparison, allowing us to detect a difference within socio-economic strata in a sample with
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22 modest size. The GEE model uses a binomial family function, a probit link function, and an
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24 exchangeable correlation structure to address the binary outcome variable and correlation among
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26 the longitudinal follow-ups of the respondents. There is no particular order effect in the repeated
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28 measures in this analysis, as patients can report CRN intermittently, and the research has shown
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30 patients are not always persistent in CRN.¹⁷ In this analysis, the value of the age variable
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32 increases by two years for each respondent for each round of surveys from 2004 to 2014. Our
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34 examination of the population-averaged effect of each risk factor on CRN gives us further
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36 evidence about the relationship between age and CRN and about the offsetting effects among
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38 other variables held constant.
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44 *Covariates*

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46 These covariates included the socio-demographics gender, race, and ethnicity. Since
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48 insurance status has been found an important predictor for CRN,¹⁸ we included a set of indicator
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50 variables for those who were enrolled in Medicare, Medicaid, other types of public insurance,
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52 private insurance, and no insurance in each round of the survey, which changed over time.
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3 Enrollment in Medicaid would indicate that they were at the lowest rung of the economic ladder,
4 since Medicaid is a means-tested, state-sponsored public insurance program for those who meet
5 the poverty level defined by each state. Research has also shown those with Medicare-Medicaid
6 dual eligibility (dual eligible) can have high CRN rates despite the additional insurance coverage,
7 likely due to the fact that those at the bottom of the economic ladder are highly sensitive to the
8 out-of-pocket payment or to non-monetary factors.¹⁹ Hence we included an indicator variable of
9 Medicare-Medicaid dual eligibility in each round. The inclusion of Medicare, Medicaid,
10 Medicare-Medicaid dual eligibility, and other insurance status variables will tease out the
11 enabling effect of health insurance on overcoming resource limitations for the poor. Although
12 not all respondents were eligible for Medicare, and a significant fraction of Medicare
13 beneficiaries had creditable drug coverage and did not enroll in the Medicare Part D outpatient
14 prescription drug program,²⁰ we included one additional indicator variable for Part D enrollment
15 at each round between 2006 and 2014 to further control potential confounding. We further
16 created an indicator variable for the year of 2004 prior to the institution of Part D.
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19 We also included two variables on functional status: limitations in Activities of Daily Living
20 (ADLs), and Instrumental Activities of Daily Living (IADLs) in each round of surveys.^{21,22}
21 These two variables measure the number of limitations in performing tasks such as dressing,
22 bathing, eating, toileting, getting out of bed, and walking (ADLs), and preparing meals,
23 shopping, managing money, and taking phone calls (IADLs). Research has also that functional
24 status is an important factor influencing CRN.²³ We also included a set of comorbid conditions
25 including diabetes, heart disease, stroke, and cancer in each round of surveys. These conditions
26 are known to have high disease burden for patients in terms of both the need for continuous
27 medical care and the high costs of medication treatments.¹⁸
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3 HRS has a rich set of questionnaires on sources of income and given that many of the elderly
4 are already in retirement and wage income would have been a poor proxy, we first created one
5 variable for total income, including wages, pensions, unemployment benefits, SS income, and
6 income from investments and financial assets for each patient. (See Appendix I for a list of
7 sources of income). Because not every income-related variable is measured on a monthly basis,
8 we extrapolated these variables to its annual amount. Because not all respondents reported
9 income (which is common in social science research,²⁴) we created one dummy variable
10 indicating those who did not report income.
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22 We compared the demographic variables, insurance status, and comorbid conditions for each
23 cohort in 2004 and 2014 respectively, using regression analyses. Specifically, the p-values were
24 for the parameter estimates of the year of 2014 compared to the year of 2004, with general linear
25 regressions for continuous variables including age and functional status, and logistic regressions
26 for binary variables including disease conditions and insurance status for time-varying variables.
27 For non-time-variant variables including gender, race, and education, Chi-squared tests were
28 performed.
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38 Finally, to adjust for Great Recession 2007-2009 which may have had a transient effect on
39 CRN, we created an indicator variable for the years of 2008 and 2010 controlling for this secular
40 event during and immediately after the recession. All analyses were weighted using 2004 sample
41 weight to reflect the highly stratified sample design of HRS and draw inferences to the
42 population. The analyses were conducted using Stata Version 14 (StataCorp, College Station,
43 Texas 77845, USA).
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51 *Patient and Public Involvement*

52 No patient involved.
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Results

Table 1 shows the demographics, insurance status, functional status, and comorbid conditions at the baseline of 2004 and at the end of follow-up of 2014, for the three cohorts (baby boomers, the silent generation, and the greatest generation, with 1,925, 2,839, and 2,666 respondents representing 12.3 million, 8.2 million, and 7.7 million people in 2004, respectively). All three generational cohorts had a higher prevalence of diabetes, cancer, heart conditions, stroke, a higher percentage of respondents with Medicare-Medicaid dual eligibility and lower percentage with private insurance in 2014 compared to 2004 ($p<0.05$). There were higher numbers of limitations in IADL among the silent generation and the greatest generation ($p<0.01$) but not in the baby boomers in 2014 compared to 2004. There was an increase in percentage of people who did not report income among the silent generation and the greatest generation from 2004 to 2014 ($p<0.01$), respectively, although the income reported were not statistically significantly different in the baby boomers and the silent generation, and marginally significant in the greatest generation ($p=0.07$).

Table 1. Socio-economic and health characteristics of the study sample.

	Age 50-54 in 2004 (Baby Boomers)		P-value	Age 65-69 in 2004 (The Silent Generation)		P-value	Age 80+ in 2004 (The Greatest Generation)		P-value
	2004	2014		2004	2014		2004	2014	
Total N: sample (weighted)	1,925 (12,312,762)	1,750 (11,243,602)		2,839 (8,189,832)	2,113 (6,228,691)		2,666 (7,709,927)	529 (1,865,348)	
CRN (% of total)	14.38	10.66	<0.01	8.05	5.31	<0.01	4.64	1.93	<0.01
<i>Demographics</i>									
Mean Age (SD)	52.29 (1.29)	62.29 (1.29)	<0.01	66.93 (1.42)	76.90 (1.40)	<0.01	84.56 (3.93)	72.80 (2.61)	<0.01
Male N (%)	5,711,903 (46.39)	5,071,821 (45.11)	<0.01	3,750,730 (45.80)	2,708,071 (43.48)	<0.01	2,865,953 (37.17)	549,748 (29.61)	<0.01

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Race									
White N (%)	9,546,207 (77.53)	8,770,743 (78.01)	<0.01	6,721,672 (82.07)	5,145,524 (82.61)	<0.01	6,722,307 (87.2)	1,648,583 (88.8)	<0.01
Black N (%)	1,366,186 (11.10)	1,157,880 (10.30)		730,263 (8.92)	501,363 (8.05)		563,630 (7.3)	123,727 (6.7)	
Other N (%)	457,827 (3.72)	431,097 (3.83)		176,414 (2.15)	143,938 (2.31)		82,439 (1.1)	3,734 (0.7)	
Hispanic N (%)	942,542 (7.66)	883,882 (7.86)		561,483 (6.86)	437,866 (7.03)		341,551 (4.4)	70,304 (3.79)	
High School Degree N (%)	10,427,873 (85.58)	9,652,366 (86.74)	<0.01	6,004,735 (73.36)	4,800,912 (77.13)	<0.01	5,104,259 (66.2)	1,382,472 (74.5)	<0.01
<i>Income</i>									
Did not report income N(%)	5,613,276 (45.59)	5,727,345 (46.52)	0.48	3,353,191 (40.94)	4,237,951 (51.75)	<0.01	1,700,631 (22.06)	6,366,197 (82.57)	<0.01
Mean Total Income (SD)	54,945 (117,001)	55,134 (134,558)	0.51	34,756 (73,000)	30,597 (50,565)	0.49	17,825 (69,859)	23,192 (22,520)	0.07
<i>Health Insurance status</i>									
Medicare N (%)	719,451 (5.85)	1,873,388 (16.72)	<0.01	7,725,548 (94.54)	6,080,594 (97.94)	<0.01	7,551,255 (98.27)	1,783,088 (96.82)	0.02
Medicaid Only N (%)	802,056 (6.53)	907,830 (8.10)	0.09	761,018 (9.32)	633,493 (10.26)	0.32	741,106 (9.68)	376,197 (20.77)	<0.01
Dual Eligible N (%)	262,570 (2.14)	447,280 (4.0)	<0.01	668,917 (8.20)	620,016 (10.04)	0.04	697,373 (9.11)	345,825 (19.09)	<0.01
Private Insurance N (%)	9,451,878 (76.76)	8,065,905 (71.92)	<0.01	5,136,278 (62.86)	2,797,509 (45.24)	<0.01	5,025,727 (65.64)	797,828 (44.76)	<0.01
Other Public Insurance N (%)	442,188 (3.60)	594,505 (5.29)	0.03	582,939 (7.13)	473,038 (7.63)	0.55	387,785 (5.05)	118,750 (6.44)	0.27
No Insurance N (%)	1,562,386 (12.70)	1,025,268 (8.34)	<0.01	58,174 (0.71)	18,372 (0.22)	0.05	14,157 (0.18)	17,155 (0.22)	0.03
Medicare Part D	0 (0)	599,798 (47.22)	-	0 (0)	2,090,310 (52.14)	-	0 (0)	661,142 (35.62)	-
<i>Functional status</i>									
Activities of Daily Life N (SD) (dress, bath, walk, eat, bed,	1.02 (1.91)	1.10 (1.94)	0.14	1.14 (1.96)	1.37 (2.05)	<0.01	1.36 (1.94)	1.19 (2.27)	<0.01

toilet) limitations									
Instrumental Activities of Daily Life N (SD) (meal, shop, phone, money) limitations	0.16 (0.50)	0.20 (0.62)	0.60	0.26 (0.66)	0.41 (0.91)	<0.01	0.85 (1.24)	1.82 (1.65)	<0.01
<i>Comorbid condition</i>									
Cancer N (%)	679,167 (5.56)	1,224,613 (10.98)	<0.01	1,250,817 (15.46)	1,390,602 (22.55)	<0.01	1,601,000 (21.1)	463,700 (25.4)	0.05
Diabetes N (%)	1,593,935 (13.04)	2,510,207 (22.50)	<0.01	1,706,534 (21.09)	1,788,997 (29.01)	<0.01	1,268,614 (16.8)	387,277 (21.2)	0.03
Heart Condition N (%)	1,399,076 (11.44)	2,052,001 (18.39)	<0.01	1,939,777 (23.97)	2,184,922 (35.42)	<0.01	3,141,721 (41.5)	897,113 (49.21)	<0.01
Stroke N (%)	310,709 (2.54)	542,715 (4.86)	<0.01	436,577 (5.39)	594,572 (9.64)	<0.01	972,042 (12.8)	392,876 (21.6)	<0.01

Legend: the numbers were weighted using 2004 HRS sample weight except the first row representing the sample. The p-values were for the parameter estimators of the year of 2014 compared to the year of 2004, with general linear regressions for continuous variables and logistic regressions for binary time-varying variables. For time-invariant variables including gender, race, and education, Chi-square tests were performed.

Figure 1 shows the observed CRN rates and their associated 95% confidence intervals by generational cohorts. There is a downward sloping of trend in CRN rates in each cohort over time despite small bumps in 2010 after the Great Recession. Figure 2 shows the adjusted CRN rates and their associated 95% confidence intervals by three generational cohorts controlling for demographics, health insurance status, disease conditions, functional status, and pre-Part D and Great Recession indicators. A downward sloping trend in CRN rates prevailed in each cohort over time.

Figure 1

Figure 2

Table 2 shows the population-averaged estimates of age effect along with other risk factors for the three generational cohorts. Since the GEE analyses were based on log link function and binary outcome, the coefficients can be interpreted as the percentage change in the likelihood of CRN due to a unit of change in the independent variables when the estimates are small. For each one-year increase in age, the likelihood of reporting CRN decreased 2% ($p=0.01$), 3% ($p<0.01$), and 2% ($p=0.02$) among baby boomers, the silent generation, and the greatest generation, respectively. In addition, women were more likely to report CRN ($p<0.01$, $p<0.01$, and $p=0.05$), respectively; and compared to White respondents, Black respondents were more likely to report CRN in all three generational cohorts ($p<0.01$). Higher income was associated with lower likelihood of reporting CRN among the cohorts of baby boomers and the silent generation ($p<0.01$, respectively), but not in the greatest generation. There were variabilities among the relationships between CRN and the various insurance statuses by generational cohort, and in general, insurance status was less likely to be statistically significant in the greatest generation. Having diabetes or heart conditions was associated with a higher likelihood of reporting CRN among the baby boomers ($p<0.01$) and the silent generation ($p<0.01$), but not the greatest generation. Similarly, a high number of deficiencies in IADLs was associated with a higher likelihood of reporting CRN among the baby boomers ($p=0.01$) and marginally among the silent generation ($p=0.09$), but not in the greatest generation.

Table 2. Association between Age, Other Risk Factors and CRN from Generalized Estimating Equation for Generational Cohorts from 2004 to 2014.

	Age 50-54 in 2004 (Baby Boomers)				Age 65-69 in 2004 (The Silent Generation)				Age 80+ in 2004 (The Greatest Generation)			
	Coef.	P>z	[95% Conf.]		Coef.	P>z	[95% Conf.]		Coef.	P>z	[95% Conf.]	
Age	-0.02	0.01	-0.03	0	-0.03	<0.01	-0.04	-0.02	-0.02	0.02	-0.04	0

Female	0.32	<0.01	0.21	0.43	0.26	<0.01	0.16	0.36	0.41	0.05	0	0.32
White	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Black	0.23	<0.01	0.10	0.36	0.24	<0.01	0.11	0.37	0.41	<0.01	0.20	0.62
Other Race	0.04	0.80	-0.25	0.33	-0.10	0.53	-0.42	0.22	-0.33	0.19	-1.32	0.25
Hispanic	-0.10	0.21	-0.26	0.06	0.12	0.17	-0.05	0.28	0.33	0.16	-0.07	0.44
Income	-0.03	<0.01	-0.06	-0.01	-0.05	<0.01	-0.07	-0.03	-0.11	0.84	-0.06	0.05
Not reporting income	-0.28	<0.01	-0.40	-0.15	-0.21	<0.01	-0.32	-0.10	-0.06	0.08	-0.34	0.02
High School	-0.36	<0.01	-0.51	-0.21	-0.13	0.02	-0.24	-0.02	-0.05	0.53	-0.20	0.10
Medicare	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Medicaid	-0.15	0.19	-0.38	0.07	-0.20	0.39	-0.65	0.26	0.31	0.13	-0.10	0.79
Dual eligibility	-0.25	0.07	-0.52	0.02	0.12	0.61	-0.34	0.58	-0.10	0.09	-0.87	0.06
Uninsured	0.27	<0.01	0.09	0.46	0.19	0.34	-0.20	0.57	0.31	0.74	-0.63	0.88
Private Insurance	-0.15	0.07	-0.33	0.02	-0.11	0.01	-0.19	-0.02	-0.11	0.10	-0.25	0.02
Other Public Insurance	-0.16	0.24	-0.42	0.11	-0.42	<0.01	-0.63	-0.21	-0.09	0.13	-0.66	0.08
Part D	0.22	0.04	0.01	0.43	0.10	0.02	0.01	0.19	0.06	0.46	-0.09	0.20
Diabetes	0.35	<0.01	0.24	0.46	0.19	<0.01	0.07	0.30	0.32	0.88	-0.19	0.23
Cancer	-0.03	0.74	-0.18	0.13	0.10	0.09	-0.02	0.21	-0.04	0.63	-0.20	0.12
Heart	0.25	<0.01	0.13	0.37	0.20	<0.01	0.10	0.30	0.11	0.10	-0.02	0.25
Stroke	-0.03	0.83	-0.30	0.24	0.07	0.41	-0.09	0.23	0.11	0.14	-0.05	0.32
ADL Deficiency	0	0.93	-0.02	0.02	0.03	<0.01	0.01	0.04	0.01	0.46	-0.02	0.04
IADL Deficiency	0.16	<0.01	0.09	0.22	0.04	0.09	-0.01	0.09	0.01	0.60	-0.04	0.07
Before Part D	0.04	0.43	-0.07	0.16	0.03	0.64	-0.08	0.13	0.02	0.14	-0.04	0.27
Great Recession	0.05	0.16	-0.02	0.12	0.02	0.54	-0.05	0.09	-0.03	0.61	-0.15	0.09

Legend: Results from Generalized Estimating Equation with CRN as binary outcome and weighted using 2004 HRS sample weights. ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living. Income was re-scaled to \$10,000s.

Discussion and Conclusions

There was a clear, persistent downward trend in CRN prevalence rates in all three generational cohorts between 2004 and 2014 (Figure 1 and 2), despite transient impact by the Great Recession after 2008. After controlling for other risk factors including gender, race, ethnicity, income, insurance status, comorbid conditions, and functional status, aging was significantly negatively associated with CRN in all three generational cohorts.

Such a steady decrease in CRN rates was accompanied by increasing limitations in functional status in the older age and an increasing prevalence of comorbid conditions, reflecting heightened frailty and disease burden in all three cohorts as they aged. There was an increase in Medicaid enrollment in the greatest generation and Medicare-Medicaid dual eligibility in all three cohorts, which likely provides protection from CRN. However, even after adjusting for Medicaid, dual eligibility and all other insurance variables, there is still a clear pattern of decreasing CRN as the population ages.

This “paradox” of decreasing CRN rates among old Americans as they age, despite bearing a higher disease burden and requiring a higher consumption of medications along with fixed or decreasing economic resources, seems to be robust, persisting through a series of controls for confounding factors. One possible explanation is that as the population ages and faces a shorter remaining life-span, the value of medication may change, resulting in the population changing their consumption bundle and devoting more resources to medication use. Such a change in their consumption bundle will inevitably constrain their ability to afford other daily needs, such as housing, food, and transportation. There is little literature on this aspect of the continued loss of welfare due to longitudinally increasing pressure to pay for medications. More research is greatly needed to evaluate the adequacy of social policy to help the elderly cope with increasing demand

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3 for medications as they age. When CRN was examined longitudinally, one recent study
4 suggested that younger age is a risk factor for persistent CRN.¹⁷ The evidence from this study
5 corroborates the supposition that patients' behavior may evolve as they age.
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10 In this study, we included all observations of CRN by the respondents regardless of mortality
11 during the follow-up. Clearly there was sample attrition due to mortality for the older
12 generations. Preserving the observations of those CRN respondents who died during follow-up
13 provided a richer data set, reflecting more fully the prevalence of CRN as the population ages.
14 Nevertheless, those who were deceased might have had increased tension between medical needs
15 and other needs for daily living, and future research should be directed at examining coping
16 strategies by the elderly when they are faced with greater certainty of death.
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26 This study is limited by the fact that the HRS does not have data to examine the subjective
27 evaluation of consumption bundles in order to derive the exact cause of decreasing CRN despite
28 increasing disease burden and increased enrollment in Medicaid and dual Medicare-Medicaid.
29 Nor does the HRS allow an exhaustive examination of consumption by goods and services.
30 Future research should be directed to examine these issues and to further illuminate the changing
31 consumption patterns of the elderly. Such changes may be forced upon them when faced with
32 exhausting their life savings while their disease burden increases. Further understanding of the
33 coping mechanisms and trade-offs faced by the elderly may have profound implications for
34 social policy that aims to protect them.
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46 *Conclusion*

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49 In summary, we presented a clear case of decreasing CRN rates among three American
50 generational cohorts independent of disease burden, frailty, income, and insurance status. This
51 may suggest a hidden gap in social policy as the elderly cope with increased burdens by reducing
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3 consumption of other goods and services, which may reduce their overall well-being. More
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5 research is greatly needed to understand this phenomenon and improve social policy for our
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7 aging population.
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ACKNOWLEDGEMENT

The study was presented in part at the International Health Economics World Congress, Basel, Switzerland, July 16, 2019. We are indebted to the constructive comments by the reviewer.

FUNDING STATEMENT

This study is supported in part by Chicago Center for Diabetes Translation Research (CCDTR) Pilot and Feasibility Grant (Zhang & Meltzer) (P30 DK092949), NIH 5R21AG053749 (Meltzer & Zhang), and NIH P30AG066619 (Meltzer & Zhang). The funders have no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

AUTHOR CONTRIBUTIONS

Dr Zhang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Zhang.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Zhang.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Bhaumik, Zhang.

Obtained funding: Meltzer, Zhang.

Administrative, technical, or material support: Meltzer, Zhang.

Supervision: Zhang.

COMPETING INTEREST STATEMENT

Dr. Meltzer reported receiving compensation from CVS Consultant outside the submitted work. No other disclosures were reported.

ETHICAL APPROVAL

The public use file of the Health and Retirement Study does not have human subjects, hence patient consent or approval by the Institutional Review Board is not required.

REFERENCES

1. Kaiser Family Foundation. KFF Health Tracking Poll – February 2019: Prescription Drugs. 2019. Available <https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-february-2019-prescription-drugs/>. Accessed August 14, 2020.
2. Morgan SG, Lee A. Cost-related non-adherence to prescribed medicines among older adults: a cross-sectional analysis of a survey in 11 developed countries. *BMJ Open* 2017;7:e014287.
3. Gellad WF, Grenard J, McGlynn EA. A review of barriers to medication adherence: a framework for driving policy options. RAND Corporation, 2009. Available at: http://www.rand.org/pubs/technical_reports/TR765.html. Accessed March 1, 2019.
4. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004; 42:200-9.
5. National Council on Patient Information and Education. Enhancing prescription medicine adherence: a national action plan. 2007. Available at http://www.talkaboutrx.org/documents/enhancing_prescription_medicine_adherence.pdf. Accessed February 4, 2017.
6. Tamblyn R, Laprise R, Hanley JA, Abrahamowicz M, Scott S, Mayo N, Hurley J, Grad R, Latimer E, Perreault R, McLeod P, Huang A, Larochelle P, Mallet L. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001; 285:421–429.
7. Mojtabai R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff*. 2003; 22(4):220–229.
8. Heisler M, Langa KM, Eby EL, Fendrick AM, Kabeto MU, Piette JD. The health effects of restricting prescription medication use because of cost. *Med Care*. 2004; 42:626–634.
9. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006; 166:1836–1841.
10. Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ, Krumholz HM, Rumsfeld JS. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Arch Intern Med*. 2006; 166:1842–1847.
11. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014 Feb 20; 7:35-44.
12. Soumerai SB, Pierre-Jacques M, Zhang F, et al. Cost-related medication nonadherence among elderly and disabled Medicare beneficiaries: a national survey 1 year before the Medicare drug benefit. *Arch Intern Med*. 2006;166(17):1829-1835.
- [Dataset] 13. Health and Retirement Study. David R Weir. Sponsored by the National Institute on Aging (NIA U01AG009740) and the Social Security Administration. Data from: Public Survey Data. December 20, 2021. <https://hrsdata.isr.umich.edu/data-products/public-survey-data>
14. The US Census. The older population in the United States: 2004. Available <https://www.census.gov/data/tables/2004/demo/age-and-sex/2004-older-population.html>. Accessed August 24, 2020.

15. Pew Research Center. Six generations moving forward together. Available <https://www.pewtrusts.org/en/trend/archive/winter-2018/notes-from-the-president-six-generations-moving-forward-together>. Accessed on February 18, 2022.
16. Liang KY and Zeger S. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 73 (1): 13–22.
17. De Avila JL, Meltzer DO, Zhang JX. Prevalence and persistence of cost-related medication nonadherence among Medicare beneficiaries at high risk of hospitalization. *JAMA Netw Open*. 2021;4(3):e210498. doi:10.1001/jamanetworkopen.2021.0498
18. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med*. 2007;22(6):864-71.
19. Zhang JX, Meltzer DO. The high cost-related medication non-adherence rate among Medicare-Medicaid dual-eligible diabetes patients. *J Health Med Econ*. 2016;2(2).
20. Kaiser Family Foundation. An overview of the Medicare Part D Prescription Drug Benefit. Available at <https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/>. Accessed September 22, 2021.
21. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA*. 1963; 185:914-919.
22. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179-186.
23. Zhang JX, Meltzer DO. Risk factors for cost-related medication non-adherence among older patients with cancer. *Integr Cancer Sci Ther*. 2015;2(6):300-304.
24. Moore JC, Stinson LL, and Welniak EJ, Jr. Income measurement error in surveys: a review. Available at <https://www.census.gov/content/dam/Census/library/working-papers/1997/adrm/sm97-05.pdf>. Accessed on November 5, 2021.

Figure 1. Observed CRN Rates by Generational Cohort 2004-2014

Legend: the numbers were weighted using 2004 HRS sample weight.

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3 Figure 2. Adjusted CRN Rates by Generational Cohort 2004-2014
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6 Legend: The numbers were weighted using 2004 HRS sample weight. The adjusted values of
7 CRN rates were derived from the generalized estimating equations controlling for demographics,
8 health insurance status, disease conditions, functional status, and pre-Part D and Great Recession
9 indicators in each generational cohort.
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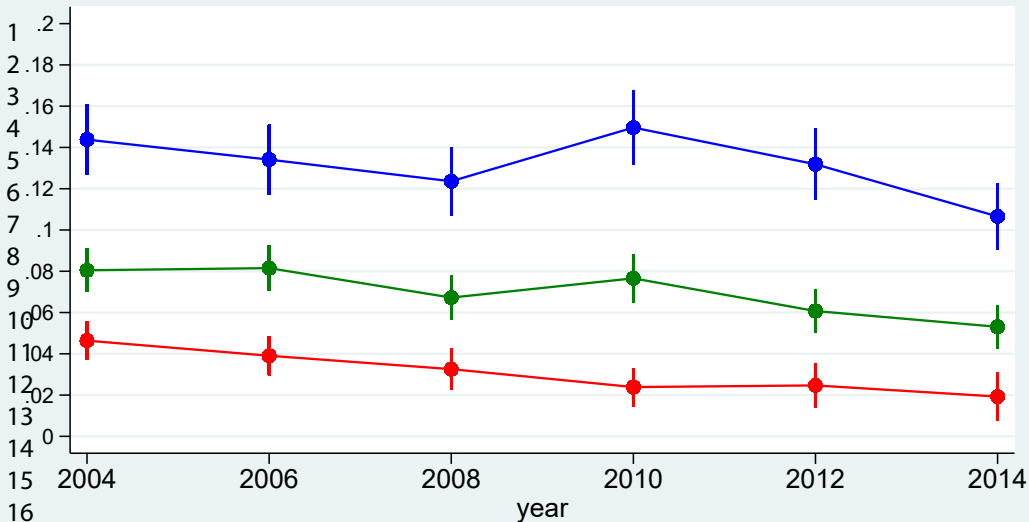
For peer review only

Appendix I. Source of Income

For peer review only

Observed CRN Rates by Generational Cohort 2004-2014

(Means and 95% CI)

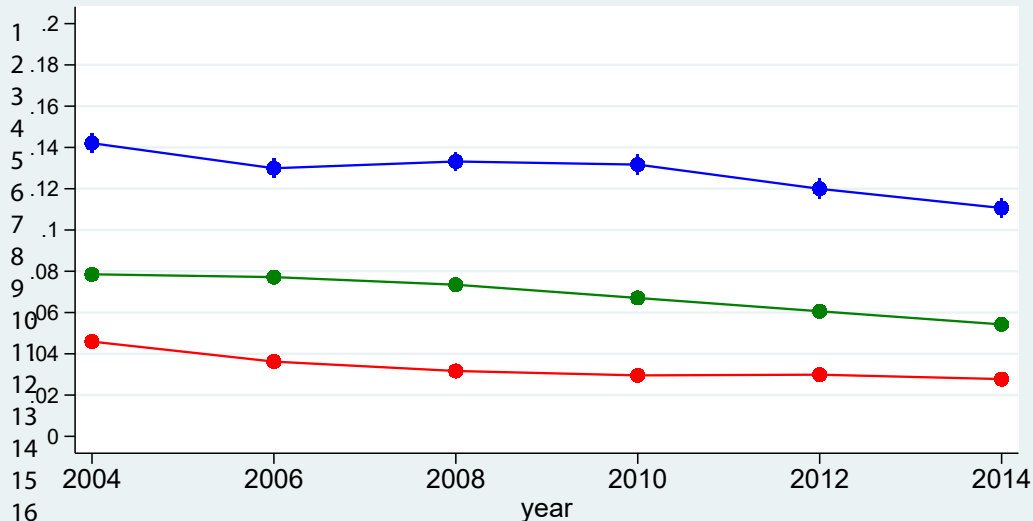


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— Baby Boomer — The Silent Generation
— The Greatest Generation

Adjusted CRN Rates by Generational Cohort 2004-2014

(Means and 95% CI)



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— Baby Boomer — The Silent Generation
— The Greatest Generation

Appendix I. Source of Income

Economic Variables
SOCIAL SECURITY INCOME
SUPPLEMENTAL SECURITY INCOME
AMOUNT FROM WORK SELF EMPL LCY
AMOUNT FROM WAGES AND SALARY LCY
AMOUNT FROM PROF PRAC OR TRADE LCY
AMOUNT FROM TIP BONUS COMMISSION LCY
AMOUNT FROM WORK 2ND JOB LCY
AMOUNT FROM UNEMPLOYMENT - LCY
AMOUNT FROM WORKERS COMP LCY
AMOUNT FROM WELFARE LCY
INC FROM OTHER IRA ANNUITY AMT
OTHER PENSIONS
OTHER ANNUITIES
STOCK INCOME AMOUNT - LCY
BOND INCOME AMOUNT - LCY
CDS INCOME AMOUNT - LCY
OTHER ASSET INCOME AMOUNT
OTHER SOURCES OF INCOME AMOUNT - LCY
VETERAN BENEFITS
AMOUNT RECEIVED FROM PENSION
AMOUNT FROM ANNUITY
AMOUNT FROM FOOD STAMPS

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

	Reporting Item	Page Number
Title and abstract		
Title	#1a Indicate the study's design with a commonly used term in the title or the abstract	1

1	Abstract	#1b	Provide in the abstract an informative and balanced summary	2
2				
3				
4			of what was done and what was found	
5				
6	Introduction			
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8				
9				
10	Background /	#2	Explain the scientific background and rationale for the	4
11				
12	rationale		investigation being reported	
13				
14				
15	Objectives	#3	State specific objectives, including any prespecified	5
16				
17			hypotheses	
18				
19				
20	Methods			
21				
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23				
24	Study design	#4	Present key elements of study design early in the paper	5
25				
26				
27	Setting	#5	Describe the setting, locations, and relevant dates, including	6
28				
29			periods of recruitment, exposure, follow-up, and data	
30			collection	
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34	Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of	6
35				
36			selection of participants. Describe methods of follow-up.	
37				
38				
39	Eligibility criteria	#6b	For matched studies, give matching criteria and number of	6
40				
41			exposed and unexposed	
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43				
44				
45	Variables	#7	Clearly define all outcomes, exposures, predictors, potential	7
46				
47			confounders, and effect modifiers. Give diagnostic criteria, if	
48				
49			applicable	
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52				
53	Data sources /	#8	For each variable of interest give sources of data and details	7,8,9
54				
55	measurement		of methods of assessment (measurement). Describe	
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57			comparability of assessment methods if there is more than	
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one group. Give information separately for for exposed and unexposed groups if applicable.

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6	Bias	#9	Describe any efforts to address potential sources of bias 7
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9	Study size	#10	Explain how the study size was arrived at 10
10			
11			
12	Quantitative	#11	Explain how quantitative variables were handled in the 7,8,9
13			
14	variables		analyses. If applicable, describe which groupings were
15			chosen, and why
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19	Statistical	#12a	Describe all statistical methods, including those used to
20			control for confounding
21	methods		
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31	Statistical	#12b	Describe any methods used to examine subgroups and
32			interactions
33	methods		
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39	Statistical	#12c	Explain how missing data were addressed
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41	methods		
42			9
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45			
46	Statistical	#12d	If applicable, explain how loss to follow-up was addressed
47			
48	methods		
49			8, 12
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52	Statistical	#12e	Describe any sensitivity analyses N/A
53			
54	methods		
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1 **Results**

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- 3
- 4 Participants [#13a](#) Report numbers of individuals at each stage of study—eg
- 5
- 6 numbers potentially eligible, examined for eligibility,
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- 8 confirmed eligible, included in the study, completing follow-
- 9
- 10 up, and analysed. Give information separately for for
- 11
- 12 exposed and unexposed groups if applicable. 9
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- 16 Participants [#13b](#) Give reasons for non-participation at each stage N/A
- 17
- 18
- 19 Participants [#13c](#) Consider use of a flow diagram N/A
- 20
- 21
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- 25
- 26 Descriptive data [#14a](#) Give characteristics of study participants (eg demographic,
- 27
- 28 clinical, social) and information on exposures and potential
- 29
- 30 confounders. Give information separately for exposed and
- 31
- 32 unexposed groups if applicable. 9
- 33
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- 36 Descriptive data [#14b](#) Indicate number of participants with missing data for each
- 37
- 38 variable of interest 6, 9
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- 44 Descriptive data [#14c](#) Summarise follow-up time (eg, average and total amount) 7
- 45
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- 50 Outcome data [#15](#) Report numbers of outcome events or summary measures
- 51
- 52 over time. Give information separately for exposed and
- 53
- 54 unexposed groups if applicable. 10
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- 1 Main results [#16a](#) Give unadjusted estimates and, if applicable, confounder-
 2 adjusted estimates and their precision (eg, 95% confidence
 3 interval). Make clear which confounders were adjusted for
 4 and why they were included 10, 16, 17, 18, 22, 23
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 11 Main results [#16b](#) Report category boundaries when continuous variables were
 12 categorized N/A
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 16 Main results [#16c](#) If relevant, consider translating estimates of relative risk into
 17 absolute risk for a meaningful time period N/A
 18
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 25 Other analyses [#17](#) Report other analyses done—eg analyses of subgroups and
 26 interactions, and sensitivity analyses 10
 27
 28
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 30 **Discussion**
 31
 32
 33 Key results [#18](#) Summarise key results with reference to study objectives 11
 34
 35
 36 Limitations [#19](#) Discuss limitations of the study, taking into account sources
 37 of potential bias or imprecision. Discuss both direction and
 38 magnitude of any potential bias. 12
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 44 Interpretation [#20](#) Give a cautious overall interpretation considering objectives,
 45 limitations, multiplicity of analyses, results from similar
 46 studies, and other relevant evidence. 11
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 51 Generalisability [#21](#) Discuss the generalisability (external validity) of the study
 52 results 12
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 57 **Other Information**
 58
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1 Funding [#22](#) Give the source of funding and the role of the funders for the
2
3 present study and, if applicable, for the original study on
4
5 which the present article is based 13
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7

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