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Does a multimethod approach improve identification of medication nonadherence in adolescents with chronic kidney disease?

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Abstract

Background—Medical provider assessment of nonadherence is known to be inaccurate.

Researchers have suggested using a multimethod assessment approach; however, no study has demonstrated how to integrate different measures to improve accuracy. This study aimed to determine if using additional measures improves the accurate identification of nonadherence beyond provider assessment alone.

Methods—Eighty-seven adolescents and young adults (AYAs), age 11–19 years, with chronic kidney disease (CKD) [stage 1–5/end-stage renal disease (ESRD)] and prescribed antihypertensive medication, their caregivers, and 17 medical providers participated in the multisite study. Five adherence measures were obtained: provider report, AYA report, caregiver report, electronic medication monitoring (MEMS), and pharmacy refill data [medication possession ratio (MPR)]. Concordance was calculated using kappa statistic. Sensitivity, specificity, positive predictive power, and negative predictive power were calculated using MEMS as the criterion for measuring adherence.

Results—There was poor to fair concordance ($\kappa = 0.12$ – 0.54), with 35–61% of AYAs classified as nonadherent depending on the measure. While both providers and MEMS classified 35% of the AYAs as nonadherent, sensitivity (0.57) and specificity (0.77) demonstrated poor agreement between the two measures on identifying which AYAs were nonadherent. Combining

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Compliance with ethical standards

Caregivers and AYAs 18 years old provided informed consent, and AYAs <18 years old gave assent to join a 2-year longitudinal study to assess antihypertensive medication adherence.

The Institutional Review Boards at all three institutions approved the study.

Conflict of interest The authors declare that they have no conflict of interest.

provider report of nonadherence and MPR < 75% resulted in the highest sensitivity for identifying nonadherence (0.90) and negative predictive power (0.88).

Conclusions—Nonadherence is prevalent in AYAs with CKD. Providers inaccurately identify nonadherence, leading to missed opportunities to intervene. Our study demonstrates the benefit to utilizing a multimethod approach to identify nonadherence in patients with chronic disease, an essential first step to reduce nonadherence.

Keywords

Antihypertensive; Adherence; Measures; Pediatric; Provider perception; Concordance

Introduction

Between \$68 and \$150 billion of avoidable health care costs have been attributed to nonadherence in the USA annually while improved adherence has been shown to result in cost saving and is associated with lower morbidity [1–3]. Adherence, as defined by the World Health Organization project on treatment adherence, is “the extent to which a person’s behavior—such as taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed upon recommendations from a health care provider” [4]. While an 80% threshold for adherence is regularly used across diseases, different measures use various cutoffs and each health outcome of interest may have a distinct threshold for predictive accuracy [5, 6]. Medication nonadherence in children and adolescents with chronic disease is highly prevalent, estimated to be 50–88% [7]. Children and adolescents with chronic disease and complex medication regimens are most at risk for adverse outcomes related to nonadherence, which is likely due to the impact on lifelong morbidity and mortality [8]. Additionally, adolescents/young adults are at the highest risk for nonadherence. This increased risk is multifactorial in origin, related to evolving identity and autonomy, decreasing parental/guardian oversight, influence of peers, and incompletely developed executive functioning skills. In children and adolescents with chronic kidney disease (CKD), poor adherence to antihypertensive and antiproteinuric medications can lead them to more quickly progress to end-stage renal disease (ESRD). Interestingly, the prevalence of medication nonadherence in children with earlier stages of CKD has not been well described despite concern about its impact on health outcomes including accelerated progression to ESRD and transplant [9–11].

With such a prevalent group of patients at risk for unfavorable outcomes related to poor adherence, there is a need to develop an effective approach to improve adherence. At the forefront in this process are medical providers who are responsible for identifying which patients are nonadherent. Few studies have examined the accuracy of providers in identifying nonadherence. Having correct knowledge of a patient’s level of adherence will better equip providers to target and implement interventions for patients most at risk for poor health outcomes.

There are several strategies for assessing medication adherence; however, there is currently no gold standard method [12–14]. Objective measures, including pill counts, pharmacy refill data, and electronic monitoring systems, and subjective measures, including medical

provider estimates and patient self-report, are used to assess adherence. Unfortunately, each approach comes with its own set of strengths and challenges [14,15]. While objective measures are free of biases, the technology adds cost, does not directly assess medication intake, and is subject to malfunctioning. Conversely, subjective measures can be practical and cost-conscious, but they are highly subject to biases such as social desirability, and response demands, such as accurately recalling past behavior [15]. In practice, most providers rely solely on their clinical impression formed during a patient encounter [16].

Several studies have compared physicians' estimates of patient adherence to either self-reported adherence or objective measures in adult patients with chronic diseases such as cystic fibrosis, HIV, inflammatory bowel disease, mental illness, hypertension, and osteoporosis [17–25]. Each of these studies has demonstrated that physicians consistently underestimate patient nonadherence. Even in kidney transplant patients where adherence is paramount and drug assays are common, providers underestimated nonadherence compared to patient report and biopsy-proven rejection episodes [26]. To our knowledge, only one pediatric study has been conducted and it also concluded that providers were inaccurate in estimating nonadherence for their patients with asthma [27]. Recognizing that providers are inaccurate in their adherence estimates, incorporation of additional adherence measures into clinical practice may be beneficial. However, which measures are most helpful remains to be determined.

To date, a direct comparison between multiple measures of adherence (i.e., provider report, patient report, caregiver report, and objective measures of adherence) has not been done in a pediatric chronic kidney disease population, where adherence is incredibly important as progression of CKD leads to ESRD. A direct comparison such as this provides an opportunity to derive a complimentary set of measures, both subjective and objective, with the goal of improving the accuracy of adherence assessment. This study aimed to evaluate if having additional measures of adherence that could be readily available in a clinical setting (i.e., self-report, pharmacy refill records) can improve the accuracy of identifying nonadherence beyond provider assessment alone, using electronic medication monitoring as the criterion for measuring adherence.

Methods

Participants

Participants included in this study were adolescents and young adults (AYAs) with CKD, their caregivers, and their medical providers from three academic medical centers in the Mid- Atlantic region of the USA. AYAs were eligible for the study if they had a confirmed diagnosis of CKD stages 1–5 or ESRD (including kidney transplant), were 11–19 years old at consent, and were prescribed an antihypertensive medication for at least 6 months. Exclusion criteria included inability to comprehend spoken English, developmental delay that would interfere with completion of study procedures, having a sibling enrolled in the study, current pregnancy, or unwillingness to use electronic medication monitors. Of the 128 participants enrolled in this study, 113 patients had provider-reported adherence (15 were missing provider adherence assessments due to 11 providers declining to answer the adherence item, 2 participants dropped out of study, and 2 provider-reported adherence

forms were not returned), 119 patients had electronic monitoring data (9 participants were prescribed liquid medication and did not use a MEMS cap), 118 had pharmacy refill data, 122 had AYA-reported adherence (6 participants did not complete or opted-out of the self-report measure), and 112 had caregiver-reported adherence (16 participants did not have a caregiver present during study visits). For this study, only data from participants with all five measures of adherence were included ($N=87$; 68%). The 41 excluded participants were less likely to be obese (17 vs. 35%) or have public insurance (22 vs. 44%) and more likely to have unknown insurance type (27 vs. 1%) than included participants ($p < .05$), but otherwise did not differ on any other demographic or illness characteristic. Seventeen providers from three medical centers were included.

Procedures

Caregivers and AYAs 18 years old provided informed consent, and AYAs < 18 years old gave assent to join a 2-year longitudinal study to assess antihypertensive medication adherence. Families were compensated \$100 for completing the baseline assessment that included AYA or caregiver-completed (for AYAs under 18) demographic survey and the Morisky Medication Adherence Scale (MMAS-8) [28]. AYAs and caregiver MMAS-8 self-reports were completed independently. AYAs and caregivers were seated such that they could not see each other's screens, they had headphones on, and questions were presented differently so they saw different screens at different times.

Antihypertensive medication adherence was measured for 2 weeks using a Medication Event Monitoring System (MEMS 6) TrackCap monitors (AARDEX Ltd., Union City, CA) using our established electronic monitoring protocol [15]. In addition, caregivers or participants older than 18 years provided written release for pharmacy records, and all AYA-or caregiver-identified pharmacies were contacted to provide medication records for 1 year prior to enrolling in the study. Providers completed a treatment plan form that included an item soliciting their impression of the AYA's level of adherence to antihypertensive medications.

Measures

AYA and caregiver-reported adherence—AYA and caregiver-reported adherence was assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8), one of the most commonly used self-reported measures of adherence [28]. The MMAS-8 assesses treatment-related attitudes and behaviors associated with the use of a specific medical treatment (in this case antihypertensive medications). It can be used to identify patients with adherence problems as well as to monitor adherence over time. MMAS-8 has a dichotomous yes/no response for seven items (with one point assigned for each affirmative response) and one question ("How often do you have difficulty remembering to take all your medications?") using a 5-point Likert scale ranging from 0 ("never/rarely") to 4 ("all the time"). The MMAS-8 has established good reliability as well as concurrent and predictive validity for blood pressure control [28]. In addition to continuous scores, the following adherence classifications were used based on total score: 0–6 = "nonadherent" and 6–8 = "adherent" as recommended by the developers.

Current antihypertensive medication treatment plan—A current medication treatment plan that included the name(s) of prescribed antihypertensive medication(s), strength per dose, frequency of doses, total strength per day, and start and end date was verified by the participant's nephrology provider. The current medication treatment plan served as the benchmark to which each objective measure of adherence was compared.

Provider-reported adherence—As part of the current medication treatment plan, providers were asked to estimate the participants' antihypertensive medication adherence by selecting one of five responses regarding percent of time the AYA was believed to take his/her prescribed antihypertensive medication: never (1), 1–24% (2), 25–49% (3), 50–74% (4), or 75–100% (5). Adherence was dichotomized into <75% = “nonadherent” and 75% = “adherent”.

Electronic medication monitoring of adherence (MEMS)—The MEMS TrackCap is a child-resistant medication bottle cap that records the date and time of each bottle opening and closure, which is later downloaded. MEMS TrackCap monitors were placed on all antihypertensive medications. The MEMS adherence score was calculated as the actual total number of openings in the observation interval divided by the expected number of openings over the observation interval as determined by the current medication treatment plan. The maximum number of possible openings per day was truncated to the maximum frequency per day. The first and last day of data was not included in the calculation to account for quality assurance testing when attaching and removing the device. To address nonmedication use openings, we ensured that participants had at least 14 days of medications placed into the MEMS bottle and performed pill counts before and after the 2-week observation period. Based on our quality check procedures, we did not note any discrepancies between the data obtained with MEMS and the pill counts. If more than one medication was prescribed, a score was calculated separately for each medication and then averaged. In addition to continuous scores, adherence was dichotomized into < 75% = “nonadherent” and 75% = “adherent”.

Pharmacy refill adherence—To assess adherence using pharmacy data, a medication possession ratio (MPR) was calculated. This is a ratio of the sum of days' supply between interval start and end dates (days' supply/study interval) and provides the percentage of days a patient has access to their medication based on their refills. For instance, if a participant had three refills of a 30-day supply during a 6-month study period, their days' supply would be 90, the study interval would be 183, and their MPR would be 0.49. In this study, the MPR study interval started 6 months prior to the baseline visit and ended at the baseline visit; the MPR was adjusted to account for medication that was remaining from the refill prior to or after the selected 6-month period. For individuals who were prescribed more than one antihypertensive medication, individual medication MPR scores for each drug were averaged to create an overall average MPR score, which was used for this analysis. In addition to continuous scores, MPR was dichotomized into < 75% = “nonadherent” and 75% = “adherent”.

Analytic plan

The distribution of data for each measure was examined, and Spearman's rho correlation among all adherence measures was calculated. Cohen's kappa was used to evaluate agreement between dichotomized provider, caregiver MMAS-8, and AYA MMAS-8 report, MPR, and MEMS (0 = nonadherent, 1 = adherent). A kappa of < 0.40 is considered poor, 0.41–0.75 is considered fair to good, while >0.75 is considered excellent agreement [29]. To evaluate if there were differences by AYA age or recruitment site, the sample was stratified (11–14 years old and 15–19 years old) or by recruitment site, and kappas were repeated.

MEMS was selected as the criterion reference for other measures of adherence to determine if there is improved accuracy of adding other adherence measures to provider report. MEMS was chosen as the criterion reference because it is an objective measure and is viewed as one of the more reliable methods to measure adherence, but is not readily available to providers. Four separate hierarchical multiple linear regressions were calculated with AYA age, gender, and race and provider report in step 1 and either (1) caregiver MMAS-8, (2) AYA MMAS-8, (3) MPR only, or (4) caregiver MMAS-8, AYA MMAS-8, and MPR entered in step 2. The change in R^2 between provider report alone and each of the four scenarios was calculated to determine if additional measures of adherence accounted for more variance beyond provider report and demographic characteristics alone. Positive predictive value (PPV), negative predictive value (NPV), sensitivity (SEN), and specificity (SPEC) were calculated for each measure separately, using the cutpoints described in the measures description, as well as combining measures.

Results

Patient and provider sample

Table 1 provides the demographic characteristics of the participants. The sample consisted of a relatively diverse sample of AYAs in relation to ethnic background and household income. Analyses were completed using the full sample of participants and using only those with all measures of adherence, and no differences were noted; therefore, we included only those with all measures of adherence. Patients were most commonly prescribed lisinopril (94.5%) and amlodipine (43.8%). Provider demographics are also presented in Table 1. Most providers were attending nephrologists ($N=14$, 82.4%), two were nephrology fellows (11.8%), and one is a certified pediatric nurse practitioner (5.9%). The majority of providers were female and Caucasian. Providers provided adherence estimates for a median of 3 AYAs (IQR = 1–9).

Adherence measures

Table 2 shows descriptive statistics for adherence measures. A substantial portion of the sample was classified as nonadherent by at least one measure. Providers rated 57 AYAs (65.5%) as 75–100% adherent, 16 (18.4%) as 50–74% adherent, 6 (6.9%) as 25–49%, 6 (6.9%) as 1–24%, and 2 (2.3%) as never adherent. Provider-reported adherence and MEMS adherence both classified 35% of AYAs as nonadherent (although not the same AYAs as evidenced by the low kappa statistic that did not reach a threshold of 0.70), whereas caregiver MMAS-8, AYA MMAS-8, and MPR adherence measures classified between 50

and 60% as nonadherent. Mean adherence on objective measures was between 62% (MPR) and 77% (MEMS). It was surprising to find that MMAS-8 identified more nonadherence than objective measures; the issues with the MMAS-8 measuring barriers as well as behaviors may be a contributing factor.

Table 3 shows the correlations among adherence measures using Spearman's rho in the lower diagonal and kappas across measures in the upper diagonal. MPR was not significantly correlated with provider-reported adherence ($\rho = 0.16$), but all other measures of adherence were significantly correlated with each other, ranging from 0.29 to 0.60. All kappas were in the poor agreement range (< 0.40) except for agreement between AYA MMAS-8 and caregiver MMAS-8 (0.54) and provider and caregiver MMAS-8 (0.40), which could be considered fair to poor agreement. The poorest agreement occurred between MPR and caregiver MMAS-8, as well as between MPR and MEMS. The kappas were essentially the same when stratifying by AYA age (11–14 vs. 15–19 years old) or by recruitment site with no kappa being above 0.70 (data not shown). Figure 1 further depicts the poor agreement between provider-reported adherence and MEMS adherence.

Provider report, AYA age, gender, and race were significantly associated with MEMS adherence ($R^2 = 0.29$; $F = 8.24$, $p < .001$) with only provider report being a significant predictor ($\beta = 0.40$, $p < .001$). The R^2 change when adding the AYA MMAS-8 alone to the model was not statistically significant (R^2 change = .03, $p = .07$). R^2 change was significant when adding caregiver MMAS-8 only (R^2 change = .08, $p = .003$) and MPR only (R^2 change = 0.08, $p = .001$) to the initial model. When all three measures were added to the model, the R^2 change was 0.13 ($p = .001$), with provider report, caregiver MMAS-8, and MPR being significant predictors in the final model ($\beta = 0.29$ ($p = .005$), $\beta = 0.27$ ($p = .02$), and $\beta = 0.27$ ($p = .008$), respectively).

Table 4 shows that each adherence measure alone had good NPV (0.74–0.79), but combining provider report and MPR had the highest NPV (0.88). That is, when both the provider and MPR indicated that the participant was adherent, it was highly likely that MEMS data also classified the participant as adherent. Provider report alone had the highest specificity (0.77); that is, providers accurately identified adherence. In contrast, the combined provider report and MPR had the highest sensitivity (0.90); that is, it was most accurate in identifying nonadherence. None of the individual measures or combinations had good PPV (range 0.40–0.57).

Discussion

All methods of assessing adherence classified a high proportion of AYAs with CKD as nonadherent, ranging from 35 to 61%. With nonadherence likely contributing to progression of CKD and potentially worse outcomes, accurate identification of nonadherence is an essential step in implementing interventions to improve adherence.

In looking at agreement between adherence measures, we noted low agreement between the objective measures of adherence, MPR, and MEMS. Agreement between the two measures may have been low because MPR provides the maximum possible adherence (i.e., how

much medication a participant has available to them) and is based on refills over 6 months, while MEMS data was collected over 2 weeks and reflects the number of times the bottle is opened. The correlation between MEMS and MPR (0.49) is statistically significant and similar to what is reported in the literature. However, since correlation only assesses the degree of linear association between two variables and does not assess the degree of concordance of the absolute values, it is important to look at actual agreement, as we did in this study, and agreement between the two measures was low.

Providers alone were relatively good at identifying adherence, likely because they disproportionately classified the majority of participants as adherent, which conversely negatively affected their identification of nonadherent AYAs. Furthermore, although the percentage of participants identified as nonadherent by providers and MEMS were equal (35%), the participants that providers identified as nonadherent were not the same ones identified as nonadherent by MEMS. Thus, there is concern that relying solely on provider-reported adherence may lead to both misclassification and under-identification of AYAs who are nonadherent and at risk for poor health outcomes. However, combining provider report with pharmacy refill data was highly sensitive; that is, combined, they accurately identified nonadherent AYAs.

Inaccurate identification of nonadherence by providers leads to missed opportunities to intervene in this group of patients at higher risk of poor health outcomes such as accelerated progression to ESRD and kidney transplant [9–11]. This finding is consistent with existing literature on adult patients with chronic diseases that demonstrated that physicians consistently underestimate patient nonadherence [18–25]. While there are two studies in pediatric patients with asthma [27, 28] that have demonstrated physicians' inaccuracy in correctly identifying adherence, this is the first study to identify providers' inaccuracy in estimating nonadherence in pediatric patients with CKD. Similar to the studies done in pediatric patients with asthma, our study found a weak correlation between self-reported adherence and provider perception of adherence; however, our study differs in that we found that self-reported adherence was lower than the provider report, which conflicts with the studies in pediatric patients with asthma [27, 28]. Physicians' perceptions may be influenced by their desire to generally view their patients as good and also influenced by certain biases, including sex, language skills, observed behaviors, knowledge of mental health concerns, or overestimating their ability to identify nonadherence [26]. Recognizing these potential biases, there is a role for the use of additional measures of adherence to help decrease the influence of these biases and more accurately identify nonadherence. Our study demonstrates the benefit in utilizing additional measures, as there is increased sensitivity of identifying nonadherence when combining provider report and an objective measure of adherence such as MPR, as compared to provider report alone.

In a busy clinical setting, it would be ideal to utilize one adherence measure as the “gold-standard.” However, with poor or only fair agreement noted between all subjective and objective measures, other than AYA MMAS-8 and caregiver MMAS-8, a thoughtful multimethod measurement approach is needed to provide unique and accurate information regarding nonadherence. The benefit of a multimethod approach to assessing nonadherence in patients with chronic disease is supported by prior studies involving patients with cystic

fibrosis, HIV, and kidney transplantation [30–32]. While we suggest and provide evidence that a multimethod approach incorporating both provider report and an objective measure such as MPR to identify nonadherence is necessary, we recognize the limited time and resources available to providers caring for patients with CKD. Thus, it is essential to explore ways in which a multimethod approach to identifying nonadherence can be successfully implemented in a busy clinical setting. We propose that objective measures, such as MPR, be obtained through electronic medical record systems or other available methods such as linked pharmacy database systems found in integrated medical systems and prominent alerts be programmed. Medical providers should review these systems prior to a patient's clinic visit or when making treatment decisions about changing doses or medications. Arming a provider with both subjective and objective measures of adherence prior to or during a clinic visit will allow the provider to more accurately identify nonadherence by potentially minimizing physician biases and inaccurate perceptions of adherence and allowing time in clinic to provide timely interventions.

Indeed, once nonadherence is correctly identified, the next step is to develop interventions to address barriers to adherence with the goal of ultimately improving adherence. There is existing literature focused on the need for a multidisciplinary team to intervene and address barriers to adherence in real time [33]; however, little to no successful interventions for patients with CKD exist and therefore more study is needed. We suggest that both a multimethod approach to identifying nonadherence and a multimethod approach to addressing nonadherence is essential to improving medication adherence in patients with chronic disease, such as CKD.

There are several limitations to our study. The sample size is relatively small, and the study is geographically restricted to three centers from the Mid-Atlantic region. Therefore, our sample may not be representative of all patients with CKD/ESRD and their caregivers and medical providers. With the study aimed at assessing concordance between all five measures, we elected to exclude those patients that did not have all five measures completed, thus decreasing our sample size. Another limitation is the potential for providers' perceptions of patients' medication adherence to be based on different time frames from that reflected in MPR and MEMS data, as well as the time frame reflected by AYA and caregiver reports of adherence (MMAS-8). Providers were asked to estimate a patient's adherence just after the baseline visit was conducted; however, their perception of adherence could reflect a broader time frame and therefore lead to discordance with other measures. We also acknowledge that the MEMS data reflects a short time frame (2 weeks), which may have led to reactivity from participants, such that they were more adherent than typical [34]. However, if MEMS measurement had been conducted over a longer period of time and there was less reactivity, MEMS adherence would have been lower and with likely even poorer agreement between provider report and MEMS, further supporting the need to incorporate additional measures to accurately identify nonadherence. Another potential limitation of MEMS, which also applies to all the measures used in this study, is that it does not confirm ingestion of medication and therefore may overestimate adherence. Ingestible sensors that would overcome this limitation are being developed, but are not ready for use in clinical practice [35]. An additional limitation to our study is the inability to precisely account for participants using a pharmacy auto refill or early order option when calculating MPR.

However, pharmacy records reflect medications that were picked up from pharmacies and it is our experience that most people pick up medications only when they are needed even if they receive a message that a refill is ready. Another limitation, due to the small sample size, is that we did not include stratified analyses by stage of CKD or indication for antihypertensive medication (hypertension vs. proteinuria). Finally, the study was limited by the lack of a true gold standard measure of adherence, making it difficult to fully evaluate the measures of adherence included in this study.

Despite these limitations, this study, to date, is the first to directly compare provider report, AYA report, caregiver report, and objective measures of adherence in a pediatric chronic kidney disease population. Our study demonstrates that providers underestimate nonadherence and are inaccurate in their assessments when compared to self-report (AYA and caregiver) and objective measures of adherence. These findings provide evidence to support the need to incorporate a multimethod assessment approach into clinical care to identify nonadherence in patients with chronic kidney disease, an essential first step in designing and implementing successful interventions to improve medication adherence and patient outcomes.

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Fig. 1.
Provider-reported adherence vs. MEMS adherence

Table 1

Demographic and caregiver characteristics of the adolescents and young adults evaluated at the baseline visit
(N = 87)

	<i>M (SD)</i>	Number	Percentage
AYA age (years)	14.8(2.5)		
AYA race			
African American		42	48.3
Caucasian		38	43.7
Asian/Pacific Islander		4	4.6
Other/not reported		3	3.4
AYA ethnicity			
Hispanic		4	4.6
Non-Hispanic		83	95.4
AYA gender			
Male		49	56.3
Female		38	43.7
AYA health comorbidities			
End-stage renal disease		20	23.0
Hypertension diagnosis		35	40.2
Obesity		30	34.5
Number of antihypertensive medications monitored			
1		63	72
2		19	22
3		4	5
4		1	1
Household income			
0–\$24,999		14	16.1
\$25,000–\$49,999		17	19.5
\$50,000–\$99,999		25	28.7
\$100,000		31	35.6
Health insurance			
Public		38	43.7
Private		44	50.6
Military		4	4.6
Unknown/other		1	1.1
Caregiver relationship to AYA			
Mother		65	74.7
Father		22	25.3
Provider gender			
Female		13	76.5
Male		4	23.5
Provider race			

	<i>M</i> (SD)	Number	Percentage
Caucasian		11	64.7
Asian		5	29.4
African American		1	5.9

AYA adolescent and young adult

Table 2

Descriptive statistics for adherence measures among 87 adolescent and young adults with chronic kidney disease

Adherence measure	Mean (SD)	Min	Max	Nonadherent ^a N (%)
Provider report	4.38 (1.04)	1.00	5.00	30 (34.5%)
AYA MMAS-8	5.70 (1.52)	2.50	8.00	46 (52.9%)
Caregiver MMAS-8	5.68 (1.80)	1.25	8.00	44 (50.6%)
Pharmacy refills (MPR) ^b	0.62 (0.30)	0.00	1.00	53 (60.9%)
Electronic medication monitoring (MEMS) ^c	0.77 (0.24)	0.05	1.00	30 (34.5%)

AYA adolescent and young adult

^aThe following classifications were used to categorize nonadherent cases: provider report, MPR and MEMS: scores <75%; AYA and caregiver MMAS-8: scores of 0–6

^bMPR is the ratio of the sum of days' supply between interval start and end dates (days' supply/study interval). Scale 0–1

^cMEMS is the actual total number of openings in the observation interval divided by the expected number of openings over the observation interval as determined by the CMTP. Scale 0–1

Table 3

Spearman's Rho and kappa statistics for concordance across adherence measures

	Provider report	Caregiver MMAS-8	AYA MMAS-8	MPR	MEMS
Provider report	<i>Rho (k)</i> –	(0.40)	(0.28)	(0.12)	(0.34)
Caregiver MMAS-8	<i>Rho (k)</i> 0.44**	–	(0.54)	(0.19)	(0.27)
AYA MMAS-8	<i>Rho (k)</i> 0.38**	0.60**	–	(0.37)	(0.23)
Pharmacy refills (MPR)	<i>Rho (k)</i> 0.16	0.29*	0.41**	–	(0.12)
Pill bottle openings (MEMS)	<i>Rho (k)</i> 0.41**	0.46**	0.43**	0.49**	–

Note. Values below the diagonal of the table indicate Spearman's Rho correlations; values above the diagonal (in parentheses) indicate kappa statistics for agreement. Spearman's Rho was computed using continuous variables, and kappas were computed using dichotomous variables for each adherence measure (0 = nonadherent, 1 = adherent)

* $p < .01$;

** $p < .001$

Table 4

Sensitivity, specificity, PPV, and NPV of adherence measures identifying nonadherence

Crosstab between measure and gold standard (MEMS)		Sen	Spec	PPV	NPV
Provider report	MEMS				
	<75%	17	13	30	77
	75%	13	44	57	
	Total	30	57	87	
AYA MMAS-8	MEMS				
	<75%	21	25	46	78
	Nonadherent	21	25	46	78
	Adherent	9	32	41	
Caregiver MMAS-8	MEMS				
	<75%	21	23	44	79
	Nonadherent	21	23	44	79
	Adherent	9	34	43	
MPR	MEMS				
	<75%	21	32	53	74
	75%	9	25	34	
	Total	30	57	87	
Provider + caregiver MMAS-8	MEMS				
	<75%	23	27	50	81
	1 or more nonadherent	23	27	50	81
	Neither nonadherent	7	30	37	
Total	MEMS				
	<75%	30	57	87	
	Total	30	57	87	
	Total	30	57	87	

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Crosstab between measure and gold standard (MEMS)					Sen	Spec	PPV	NPV
Provider + MPR	<75%	Total	75%	Total	0.90	0.39	0.43	0.88
	for more <75% 27	62	35	62				
	Neither <75%	25	22	25				
	Total	87	57	87				

Sen sensitivity, Spec specificity, PPV positive predictive value, NPV negative predictive value