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Kimberly J. Arcoleo
Collen McGovern
Karentjot Kaur
Jill S. Halterman
Jennifer R. Mammen
University of Rhode Island, jmammen@uri.edu

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Authors

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Longitudinal Patterns of Mexican and Puerto Rican Children’s Asthma Controller Medication Adherence and Acute Healthcare Utilization
Kimberly J. Arcoleo, PhD, MPH1, Colleen McGovern, PhD, MPH, RN2, Karenjot Kaur, BA3, Jill S. Halterman, MD, MPH4, Jennifer Mammen, PhD, NP-C5, Hugh Crean, PhD1, Deepa Rastogi, MBBS, MS6, Jonathan M. Feldman, PhD3,6

1School of Nursing, 4Department of Pediatrics, School of Medicine & Dentistry, University of Rochester, Rochester, NY, USA; 2School of Nursing, University of North Carolina – Chapel Hill, Chapel Hill, NC, USA; 3Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA; 5School of Nursing, University of Rhode Island, Providence, RI, USA; 6Albert Einstein College of Medicine, Children’s Hospital at Montefiore, Bronx, NY

Corresponding Author:
Kimberly Arcoleo, PhD, MPH
Associate Professor
Associate Dean for Research
University of Rochester
School of Nursing
601 Elmwood Avenue, Box SON
Rochester, NY 14642
Email: Kimberly_arcoleo@urmc.rochester.edu

Author Contributions: CM assisted in conducting the literature review, drafting the Introduction, contributed to the interpretation of data and content of the Conclusions section, and reviewed and provided final approval for the submission. KK was responsible for cleaning the Doser adherence data and variable creation, contributed to the interpretation of data and content of the Conclusions section, and reviewed and provided final approval for the submission. JH provided substantial input on the interpretation of the results, drafting the Introduction and Conclusions sections, and reviewed and provided final approval for the submission. JM participated in drafting the Introduction and Conclusions sections, interpretation of the results and reviewed and provided final approval for the submission. HC assisted KA with the SEM and LLCA analyses, interpretation of the data, and reviewed and provided final approval for the submission. DR participated in drafting the Introduction and Conclusions sections, interpretation of the results, and reviewed and provided final approval for the submission. JF participated in the design of the main study, supervised the cleaning and variable creation from the adherence data, drafting the Introduction and Conclusions sections, interpretation of the results, and reviewed and provided final approval for the submission.

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Conflict of Interest: All authors declare no conflicts of interest, financial or otherwise.

Keywords: medication adherence, asthma, healthcare disparities
Running Head: patterns of controller medication adherence

Word Count: 3499

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Abstract

Rationale: Researchers tend to study Latinos as a single group but recent asthma research confirmed differences among Latino subgroups. Variations in controller medication adherence may be a factor in the observed health disparities between Mexican and Puerto Rican children. Adherence is not a stable phenomenon, however, there is a paucity of data on patterns of adherence, sociodemographic predictors of patterns, and variations in asthma-related acute healthcare utilization by adherence pattern among Latino sub-groups.

Objectives: Identify patterns of inhaled corticosteroid medication adherence over twelve months among Mexican and Puerto Rican children with persistent asthma; examine socio-demographic predictors of adherence patterns by ethnicity; and investigate asthma-related acute healthcare utilization based on these patterns.

Methods: We analyzed controller medication Doser data from Mexican and Puerto Rican children (n=123; ages 5-12 years) with persistent asthma who participated with their caregivers in a longitudinal, non-intervention study (Phoenix, AZ and Bronx, NY). Interview and medical record data were collected at enrollment, 3, 6, 9, and 12 months post-enrollment.

Results: 47%-53% of children had poor adherence (<50%) over each of the follow-up periods (cross-sectional). Children with lowest adherence were Puerto Rican, from non-poor families, or female. Longitudinal latent class analysis yielded 4 adherence classes: poor; moderate; declining adherence; and increasing adherence. Puerto Rican children had significantly higher odds of “Decreasing” (OR=2.86; 95% CI, 0.40 to 20.50) and “Poor” (OR=5.62; 95% CI, 1.44 to 21.90) adherence compared to Mexican children. Females had significantly greater odds of “Decreasing” (OR=4.80; 95% CI, 0.73 to 31.74) and “Poor” (OR=5.20; 95% CI, 1.77 to 15.30)
adherence group membership compared to Males. The “Decreasing” adherence group was comprised of only poor children. Children in the “Poor” adherence class had the highest mean number of acute visits and ED visits/hospitalizations across all assessment periods.

Conclusions: This study demonstrated that unique ethnicity within Latino populations may be associated with different risk levels for suboptimal controller medication adherence which may be a factor in the observed asthma health disparities between Mexican and Puerto Rican children. Increased understanding of and attention to children’s controller medication adherence patterns will provide evidence needed to identify children at highest risk for acute healthcare utilization and offer more intensive intervention using less-intensive approaches for those at low risk.

Abstract Word Count: 350
Despite evidence-based guidelines for asthma management and control (1), low asthma controller medication adherence in children persists, with minority children at greater risk of non-adherence and poor outcomes than non-minority children (2-6). Adherence to controller medications is critical and can significantly reduce exacerbations and improve asthma control (2, 7, 8). Researchers have tended to study Latinos as a single group but recent descriptive asthma research has confirmed significant heterogeneity among Latino subgroups (particularly between Mexicans and Puerto Ricans) regarding prevalence, mortality and morbidity, illness beliefs, and asthma healthcare practices (9-13). Puerto Rican children exhibit the highest rates of asthma prevalence and mortality among all ethnic groups while Mexican children have the lowest rates (9, 12). Genetic, environmental, healthcare system, and provider factors (13-15) cannot totally explain the differences between these two groups.

There is growing evidence about factors leading to non-adherence and interventions focused on improving adherence. Although an evidence-based cut-off value for good adherence (16) has not been established, rates >80% are traditionally considered acceptable (16, 17). The majority of adherence interventions primarily target children with controller medication adherence <80% assuming that children >80% at initial assessment will remain adherent. There is evidence that adherence is not a stable phenomenon (17-20), although there is a paucity of data on patterns of adherence among individuals with asthma and none within sub-groups of Latino children (21). Souverein et al. (17) examined longitudinal patterns of inhaled corticosteroid (ICS) medication initiation (21) among a sample of long term care patients (n=13,922). The results identified periods of non-adherence alternating with periods of regular ICS use. LaForest et al. (20) examined ICS adherence over 12 months among children and adults
selectively recruited for high initial adherence. The investigators noted fragmented episodes of ICS use which typically lasted several months even though all individuals were adherent at baseline (20). A better understanding of controller medication adherence patterns in children will provide evidence needed to identify individuals at highest risk for non-adherence and acute healthcare utilization and offer a more intensive intervention while using less-intensive approaches for those at low risk preventing waste of precious healthcare resources.

A literature review revealed no studies directly examining controller medication adherence between Mexican and Puerto Rican children; thus these analyses fill a critical gap in our knowledge and offer insights to factors leading to asthma health disparities between these Latino sub-groups. The objectives of these secondary analyses were to: 1) identify patterns of children’s ICS medication adherence over a 12 month assessment period in a sample of Mexican and Puerto Rican children with persistent asthma; 2) examine sociodemographic and seasonal predictors of adherence patterns and; 3) investigate asthma-related acute healthcare utilization based on these patterns. To the best of our knowledge, this was the first study to examine objectively measured longitudinal patterns of ICS medication adherence in children, explore heterogeneity in adherence patterns within a sample of Latino children, and link those patterns to clinical outcomes.

Methods

We analyzed ICS medication data from a sample of Mexican and Puerto Rican children with persistent asthma requiring daily controller medications (ages 5-12 years) who participated
with their caregivers in a longitudinal, non-intervention study (Phoenix, AZ and Bronx, NY). The main study tested an explanatory, integrated multi-factorial model investigating the interaction of individual characteristics, cultural and experiential and healthcare system factors, and social-environmental context that lead to disparities between these two Latino sub-groups. Children and caregivers were recruited from two school-based health clinics and the Breathmobile in Phoenix, Arizona and two inner-city hospital asthma clinics in Bronx, New York. A total of 267 child/caregiver dyads were enrolled in the main study. Structured interviews were administered to caregivers and shorter interviews and spirometry assessments conducted with children at enrollment and 3, 6, 9, and 12 months post-enrollment. A retrospective review of children’s medical records was completed. Objective measures of children’s ICS medication adherence were assessed by Doser devices (MediTrack Products, Hudson, MA) attached to the top of the ICS canister at baseline. Data were downloaded at each follow-up visit yielding 12 months of adherence measures. Due to differences in treatment regimen adherence between inhaled and oral and combination ICS/LABA controller medications, all children with use of oral and/or combination ICS/LABA medications were excluded (n=73) from these analyses. Two children had no record of controller or quick relief medication prescriptions. We had Doser data on a subsample of 123 of 192 children (64.1%) prescribed inhaled corticosteroids. The study was approved by the Institutional Review Boards of the Arizona State University, Phoenix Children’s Hospital, Scottsdale Healthcare and Albert Einstein College of Medicine.
**Sociodemographic Characteristics**

All enrolled participants self-identified as Mexican or Puerto Rican. We obtained child’s sex, age, and asthma duration (number of months since diagnosis); family perception of poverty; caregiver’s marital status and education; and season of interview. Due to the socio-legal climate in Phoenix, we did not ask for annual income demonstrating sensitivity to the challenges these families were facing. To assess caregivers’ perception of poverty, a measure adapted by Gore et al. (22) asked “What best describes your family’s standard of living?” Response choices ranged from 1=Very well off to 6=Poor and was dichotomized as Poor=Nearly Poor or Poor. All enrolled children/caregiver dyads were Medicaid/Medicaid-eligible and received their asthma medications free from the participating clinics.

**Seasonality**

Using each interview date, we created the season that baseline and follow-up interviews were conducted, adherence data captured, and acute asthma-related healthcare utilization occurred. Seasons were defined as: Spring=March-May; Summer=June-August; Fall=September-November; Winter=December-February.

**Clinician-rated Asthma Severity**

Clinician ratings of children’s asthma severity were conducted per clinical guidelines (1). The ratings were based on clinicians’ assessment of impairment given the caregivers’ and children’s responses to structured questions regarding daytime and nocturnal symptoms, activity
limitations, short-acting β2 agonist use for the 2-4 week period prior to the interview, spirometry, and risk of adverse events. All ratings were completed by pediatric pulmonologists.

Adherence

Doser devices were attached to the child’s ICS canister at the baseline visit. Doser data were downloaded at each assessment period (M3=baseline-month 3; M6=month 3-month 6; M9=month 6-month 9, and M12=month 9-month 12) yielding 12 months of adherence data. The Doser devices recorded the number of actuations each day for the prior 30 days. For medications where we could not attach the Doser due to built-in counters, we captured the counter data at each visit. Adherence data were cleaned per procedures outlined by McQuaid, Kopel, Klein & Fritz (23). Adherence was calculated as the # doses taken per day/# prescribed doses per day x 100. Daily adherence was truncated to 100% to account for accidental actuations (e.g., bumping in a backpack) or intentional actuations due to trying to make up for missed doses the previous day. Average adherence and adherence categories were created (<50%=Poor, 50-80%=Moderate, >80%=Good) at each time period (24).

Acute Healthcare Utilization

Children’s medical records from the recruitment site were reviewed for 12 months prior to enrollment and the 12 month study period to obtain counts of acute and ED asthma visits and hospitalizations. Asthma-related ED visits and hospitalizations were combined due to the low frequency. Because asthma-related healthcare visits may have occurred outside the child’s medical home, caregiver reports were checked against the medical record based on visit date
(± one month to account for recall errors). In cases where the medical record and caregiver dates were congruent, medical record data were used. Where there was a caregiver report but no medical record visit for that date, caregiver report was used. If a visit was recorded in the medical record but not reported by the caregiver, medical record data were used.

**Statistical Analyses**

Only data for children prescribed an ICS medication and who had at least 2 adherence data points were analyzed. Cross-sectional descriptive chi-square analyses examined adherence by ethnicity, child sex and age, poverty, and season. Structural equation modeling and longitudinal latent class analysis (LLCA) explored patterns of adherence over time and acute healthcare utilization by adherence class. The LLCA also examined sociodemographic characteristics (ethnicity, marital status, poverty, caregiver education, child’s age, sex, and asthma duration, and number of family members with asthma) to identify predictors of class membership. Interaction effects for ethnicity with caregiver marital status, education, poverty, and child sex were examined. Reference groups were Puerto Rican, female, non-poor, summer, and “Moderate” adherence group. Model selection was based on the log likelihood, Bayesian Information Criteria (BIC), and entropy. Models specifying 2, 3, and 4 classes were run and fit statistics compared to determine the best fitting model (25, 26). Statistical significance was set at $p<.10$, the convention for structural equation modeling and LLCA.
Results

A total of 267 child/caregiver dyads enrolled and completed baseline measures and assessments. We had adherence data for 123/192 children prescribed non-combination ICS medications (64.1%). Analyses were conducted (data not shown) to examine whether children who were missing adherence data were different from those who had adherence data based on ethnicity; recruitment site; number of family members with asthma; caregivers' marital status, education, perception of poverty, reported use of controller medication in the past month, age and sex; and child’s sex, age, asthma duration and severity. Children who were missing adherence data were more likely to not have used controller medications in the past month, had mild or severe persistent asthma, and had caregivers who were older and high school graduates. There were no differences by ethnicity.

Table 1 presents the sample characteristics by ethnic group. Puerto Rican caregivers were less likely to be married or poor and more likely to have graduated from high school. Puerto Rican children were younger, had higher clinician ratings of severe persistent asthma, and lower likelihood of caregiver-reported controller medication use in the past month compared to Mexican children.

Cross-sectional Analyses

Figure 1 illustrates cross-sectional adherence by time. Good adherence (>80%) at each time period was low (14%-23%) with the largest proportion of children demonstrating poor adherence (47%-53%). Puerto Rican children had the highest proportion of poor adherence at
each time period (63%-80%) compared to Mexican children (40%-49%) (see Figure E1A in the Online Supplement). Although a higher proportion of Mexican (19%-23%) compared to Puerto Rican children (0%-21%) had good adherence, overall, these proportions are quite low. Because all of the Puerto Rican children were enrolled at the Bronx hospital clinics, we conducted additional analyses to investigate whether adherence differences were due to ethnicity or clinic setting. A sub-group analysis was conducted comparing adherence for Mexican and Puerto Rican children enrolled at the Bronx hospital clinic sites. More Puerto Rican children in the hospital clinics had poor adherence at every time period (71%-80%) compared to Mexican children from the same clinic (33%-63%). Additionally, we examined adherence by site to determine whether adherence was lowest at the hospital-based clinics in the Bronx compared to the other sites. The school-based health centers in Phoenix actually had the lowest adherence across all assessment periods (range 10%-31%) followed by the hospital-based clinics (range 34%-38%) with the Breathmobile consistently having the highest adherence (range 50%-56%). These findings support our conclusion of ethnic differences unrelated to clinic site. Good adherence was low for both sexes ranging from 5% to 23% (see Figure E1B in the Online Supplement). Across all time periods, females demonstrated the highest proportions of poor adherence (55%-77%). At M3 and M6, more non-poor children demonstrated poor adherence compared to poor children. These differences dissipated over time (see Figure E2A in the Online Supplement). There were no seasonal differences in adherence at any time period (see Figure E2B in the Online Supplement). Similar adherence proportions were observed for younger and older children with the majority having poor adherence across all time periods (data not shown).
Longitudinal Latent Class Analysis

We tested 2, 3 and 4 class models examining adherence patterns from baseline through 12 months. Multiple imputation was used to impute missing data for the 123 children that had adherence data for at least 2 time periods. The LLCA revealed that the four class solution was the best of the three models tested. These classes of adherence are: poor (47%); moderate (31%); declining adherence (good or moderate adherence transitioning to poor adherence) (7%); and increasing adherence (poor adherence shifting to moderate or good adherence) (15%) (Figure 2). Table 2 presents the results for significant predictors of adherence class membership; ethnicity, child sex, and poverty. No differences were observed for marital status, caregiver’s education, child’s age, asthma duration, or number of family members with asthma. Puerto Rican children had significantly higher odds of being in the “Decreasing” and “Poor” adherence groups compared to Mexican children. Females had significantly greater odds of being in the “Decreasing” and “Poor” adherence groups compared to Males; no females were in the “Improving” adherence class. The “Decreasing” adherence class was comprised of only poor children and these children also had lower odds of being in the “Improving” adherence class. No interaction effects of ethnicity with caregiver marital status, education, poverty, or child sex were observed (data not shown).

Differences in asthma-related healthcare utilization (i.e., acute care visits and ED visits/hospitalizations) were examined by adherence class and modeled by assessment period across 12 months. These results are presented as forest plots (Figures 3 and 4, respectively) where the x-axis represents the mean difference and I^2 is a measure of heterogeneity between the groups. For these analyses, I^2 >50% is considered statistically significant. Because of small
class sizes and low frequency of healthcare visits, we examined effect sizes to ascertain clinically meaningful (effect size >=.20) differences between classes for acute care visits and ED visits/hospitalizations in addition to statistically significant differences. For acute visits, statistically significant heterogeneity was observed among the different adherence classes (excluding Month 9) as evidenced by I² values ranging from 63%-78%. With the exception of Month 9, small to moderate clinically meaningful differences were also noted over time (effect sizes ranging from 0.22 to 0.55) although there was no discernable pattern to these differences. Figures E3A in the Online Supplement plots the mean number of acute visits at each assessment period by adherence class. The “Moderate” adherence class had the lowest acute visits through M9 but demonstrated a large increase from M9 to M12. The “Decreasing” adherence class initially had the highest acute visits which decreased through M9 and plateaued at M12. At M3, the “Increasing” adherence class had low acute visits which peaked at M6 and then declined through M9 and M12. With the exception of M9, the “Poor” adherence class had the highest acute visits.

A different pattern emerged for ED visits/hospitalizations. Statistically significant heterogeneity between adherence classes was observed only at Month 6 and Month 9 (I²=80% and 73%, respectively). However, only the difference between the poor and moderate adherence classes was clinically meaningful (effect size=.23). At M3, all four classes had equivalent ED visits/hospitalizations. At M6, the “Poor” adherence class had significantly greater ED visits/hospitalizations compared to the remaining classes, a finding which held across M9 and M12 (Figure E3B in the Online Supplement). The “Moderate” adherence class had the lowest ED visits/hospitalizations at M6 but demonstrated steadily increasing visits
through M9 and M12. The “Increasing” adherence class exhibited steady declines in ED visits/hospitalizations from baseline through M9 which then dramatically increased at M12. The “Decreasing” adherence class had relatively stable ED visits/hospitalizations across the 12 month assessment period. Examination of the between class differences revealed clinically meaningful differences for almost all contrasts (excluding M6 increasing vs. decreasing adherence and M12 increasing vs. poor adherence) from M3 through M12 months.

Discussion

These results add to our emerging evidence on patterns of ICS medication adherence in children. Notably, in our cross-sectional analyses, few children had adherence rates consistently >80% and less than one third were classified as having moderate adherence (50%-80%). Our LLCA identified four classes of adherence with the majority (78%) classified as poor or moderate. This finding supports the tendency to focus interventions on individuals with adherence <80% using a risk/benefit approach. These results revealed that acute healthcare utilization differed by adherence class over time. Children in the “Poor” adherence class had the highest utilization across the entire 12 month period but there was an unexplained drop in acute visits between M6 and M9 which was not explained by season. The “Decreasing” adherence group had steadily declining acute visits and relatively stable ED visits/hospitalizations over the 12 month assessment period which may be due to caregivers stepping down therapy or stopping therapy when the child has been asymptomatic for a period of time. Several studies have reported that caregivers have a strong desire for their children to
be medication-free and thus, discontinue using controller medications when the child no longer “has asthma” (27, 28). As we anticipated, children in the “Moderate” adherence group also had the lowest number of acute visits through M9. An unexpected finding was a dramatic increase in acute visits between M9 and M12, similar to what we observed for the poor adherence class. Again, this was not due to seasonal effects. When the “Improving” adherence class emerged, given that this was not an intervention study, we hypothesized that possibly an ED visit or hospitalization was the “trigger” for getting back on track with the prescribed regimen and this group of caregivers intervened early enough to prevent ED visits and hospitalizations. There is some support for this as evidenced by declining acute visits from M3 through M12 and slightly declining ED visits/hospitalizations through M9. However, this group had a substantial increase in ED visits/hospitalizations from M9 to M12 months almost equaling the poor adherence class. Once more, this increase was not associated with season.

It is worth noting that evidence from prior research suggests that adherence in Latino children is strongly affected by children’s and caregiver’s symptom perception which is not highly accurate (29-31) and differs between Puerto Rican and other Latino sub-groups (32, 33); cultural beliefs about asthma and medication use (27, 28); and other socio-economic factors. This suggests close clinical monitoring of ICS medication use and development of targeted interventions to address inaccurate symptom perception and sub-optimal treatment patterns in this at-risk population. Given that pediatric adherence is heavily influenced by parental involvement, effective intervention may require tailoring to specific cultural needs at both adult (parent, grandparent) and child level.
Our study also is the first study showing that unique ethnic identity within Latino populations may be associated with different risk levels and highlights the role of socioeconomic factors. We demonstrated that Puerto Rican children were at substantially greater risk of poor adherence compared to Mexican children and that poor adherence led to the highest acute healthcare utilization across time. This supports our notion that adherence patterns may be a factor in Latino children’s asthma health disparities. Our findings are pertinent in addressing the differences in asthma burden between Mexican and Puerto Rican children. Puerto Rican children, on average, were half as adherent as Mexican children. Lack of adherence to ICS medications in our study highlights the role of these medications in the lack of bronchodilator responsiveness observed to a higher extent among Puerto Rican compared to Mexican children (36). It is unsurprising that poverty adversely affects adherence. Lack of adherence to medications in poor families is likely multifactorial. For many of these families lacking sufficient resources, purchasing controller medications may be a lower priority when there are competing demands for limited resources. Although Puerto Ricans perceived themselves as less poor than Mexicans and all study children received their ICS medications for free, they had lower adherence suggesting that factors other than poverty contributed to their lack of adherence. Higher asthma burden has been reported among female children compared to male (4, 37) and our findings confirm that with females exhibiting greater odds of decreasing and poor adherence. One explanation may be that as girls get older there is social pressure to look and act a certain way and using an inhaler may make them feel “different.”
Limitations

There are several important limitations. Objective measures of adherence were based on Doser tracking devices attached to the child’s ICS canister. The devices we used were capable of only storing the most recent 30 days of usage. Thus, we were unable to examine adherence continuously across the 12 month assessment period. Only 64% of the children had valid adherence data, thus, poor medication adherence may actually be under-estimated because this sub-sample may represent those individuals who were reliable enough to bring the medications to the visits. Additionally, several of the class sizes were small and thus, we may not have had adequate statistical power to assess longitudinal between adherence class differences. Lastly, we did not have pharmacy fill/refill data to compute the medication possession ratio or controller to total medication ratio as additional measures of adherence.

Implications and Future Research

Our findings suggest medication adherence is a major contributor to disease burden and acute healthcare utilization among urban Latino children. To the best of our knowledge, this was the first study which characterized longitudinal patterns of children’s asthma ICS medication adherence and demonstrated differing risk levels for non-adherence based on ethnicity within the Latino population. Future research should further explore these patterns and risk factors among more heterogeneous Latino samples to inform targeted adherence intervention strategies. Health technology and wearable sensors are transforming our ability to monitor adherence beyond simply counting device actuations to assessing inhaler technique and capturing clinically meaningful data such as exhaled nitrous oxide, cough rate, and respiration.
patterns which can seamlessly upload data through wireless connectivity and Smartphone apps (38). Given that a significant proportion of children did not have adherence data and our Dosers could not continuously monitor adherence, future studies should incorporate these monitoring devices to more precisely examine the intra- and inter-person variability longitudinally and minimize missing adherence data. This technology could support adherence interventions that can be tailored to different ethnic sub-groups.

**Acknowledgements**

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References


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<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver’s Age</td>
<td>34.57</td>
<td>36.00 (9.39)</td>
</tr>
<tr>
<td></td>
<td>(6.41)</td>
<td></td>
</tr>
<tr>
<td># Family Members w/Asthma</td>
<td>1.17 (0.73)</td>
<td>0.82 (1.11)</td>
</tr>
</tbody>
</table>
### Table 2. Sociodemographic Predictors of Controller Medication Adherence Class Membership

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model $\chi^2$</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improving Adherence</td>
<td>9.15</td>
<td></td>
</tr>
<tr>
<td>Mexican</td>
<td>Referent .73 (.05, 11.86)</td>
<td></td>
</tr>
<tr>
<td>Puerto Rican</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreasing Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexican</td>
<td>Referent 2.86 (.40, 20.50)</td>
<td></td>
</tr>
<tr>
<td>Puerto Rican</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexican</td>
<td>Referent 5.62 (1.44, 21.90)</td>
<td></td>
</tr>
<tr>
<td>Puerto Rican</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Child Sex</strong></td>
<td>85.07</td>
<td></td>
</tr>
<tr>
<td>Improving Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Referent 0</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreasing Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Referent 4.80 (.73, 31.74)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Referent 5.20 (1.77, 15.30)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Poverty</strong></td>
<td>99.49</td>
<td></td>
</tr>
<tr>
<td>Improving Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Poor</td>
<td>Referent .41 (.07, 2.34)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreasing Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Poor</td>
<td>Referent 0</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Poor</td>
<td>Referent .74 (.25, 2.13)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Moderate adherence is the referent group

Definition of abbreviations: CI=confidence interval; OR=odds ratio
Figure Legends:

**Figure 1.** Categorical Cross-Sectional Adherence

**Figure 2.** Longitudinal Latent Class Analysis: 4 Class Solution

**Figure 3.** Forest Plot of Longitudinal Acute Healthcare Visits by Adherence Class

**Figure 4.** Forest Plot of Longitudinal ED Visits/Hospitalizations by Adherence Class
<table>
<thead>
<tr>
<th>Study ID</th>
<th>ES (95% CI)</th>
<th>% Weight (I-V)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Month 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor vs. Decreasing</td>
<td>0.07 (-0.12, 0.25)</td>
<td>1.02</td>
</tr>
<tr>
<td>Poor vs. Moderate</td>
<td>0.23 (0.14, 0.32)</td>
<td>4.21</td>
</tr>
<tr>
<td>Poor vs. Increasing</td>
<td>0.15 (0.02, 0.28)</td>
<td>2.05</td>
</tr>
<tr>
<td>Decreasing vs. Moderate</td>
<td>0.30 (0.22, 0.38)</td>
<td>5.12</td>
</tr>
<tr>
<td>Decreasing vs. Increasing</td>
<td>0.22 (0.12, 0.32)</td>
<td>3.22</td>
</tr>
<tr>
<td>Moderate vs. Increasing</td>
<td>0.08 (0.02, 0.14)</td>
<td>10.02</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 77.5%, p = 0.000)</td>
<td>0.17 (0.13, 0.21)</td>
<td>25.65</td>
</tr>
<tr>
<td><strong>Month 6</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor vs. Decreasing</td>
<td>0.45 (-0.11, 1.01)</td>
<td>0.11</td>
</tr>
<tr>
<td>Poor vs. Moderate</td>
<td>0.55 (0.28, 0.82)</td>
<td>0.48</td>
</tr>
<tr>
<td>Poor vs. Increasing</td>
<td>0.36 (-0.03, 0.75)</td>
<td>0.22</td>
</tr>
<tr>
<td>Decreasing vs. Moderate</td>
<td>0.10 (0.02, 0.18)</td>
<td>5.00</td>
</tr>
<tr>
<td>Decreasing vs. Increasing</td>
<td>0.09 (-0.05, 0.23)</td>
<td>1.86</td>
</tr>
<tr>
<td>Moderate vs. Increasing</td>
<td>0.19 (0.11, 0.27)</td>
<td>5.73</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 63.4%, p = 0.018)</td>
<td>0.16 (0.11, 0.21)</td>
<td>13.41</td>
</tr>
<tr>
<td><strong>Month 9</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor vs. Decreasing</td>
<td>0.01 (0.01, 0.23)</td>
<td>2.94</td>
</tr>
<tr>
<td>Poor vs. Moderate</td>
<td>0.09 (0.03, 0.15)</td>
<td>11.12</td>
</tr>
<tr>
<td>Poor vs. Increasing</td>
<td>0.02 (-0.06, 0.10)</td>
<td>5.19</td>
</tr>
<tr>
<td>Decreasing vs. Moderate</td>
<td>0.03 (-0.03, 0.09)</td>
<td>10.02</td>
</tr>
<tr>
<td>Decreasing vs. Increasing</td>
<td>0.14 (0.05, 0.23)</td>
<td>4.31</td>
</tr>
<tr>
<td>Moderate vs. Increasing</td>
<td>0.11 (0.06, 0.16)</td>
<td>11.96</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 45.2%, p = 0.104)</td>
<td>0.07 (0.05, 0.10)</td>
<td>45.53</td>
</tr>
<tr>
<td><strong>Month 12</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor vs. Decreasing</td>
<td>0.27 (0.10, 0.44)</td>
<td>1.22</td>
</tr>
<tr>
<td>Poor vs. Moderate</td>
<td>0.01 (-0.09, 0.11)</td>
<td>3.56</td>
</tr>
<tr>
<td>Poor vs. Increasing</td>
<td>0.23 (0.11, 0.35)</td>
<td>2.34</td>
</tr>
<tr>
<td>Decreasing vs. Moderate</td>
<td>0.26 (0.11, 0.41)</td>
<td>1.51</td>
</tr>
<tr>
<td>Decreasing vs. Increasing</td>
<td>0.04 (-0.05, 0.13)</td>
<td>3.95</td>
</tr>
<tr>
<td>Moderate vs. Increasing</td>
<td>0.22 (0.11, 0.33)</td>
<td>2.83</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 74.6%, p = 0.001)</td>
<td>0.13 (0.09, 0.18)</td>
<td>15.41</td>
</tr>
</tbody>
</table>

Heterogeneity between groups: p = 0.000

I-V Overall (I-squared = 73.2%, p = 0.000) | 0.12 (0.10, 0.14) | 100.00 |

D+L Overall | 0.14 (0.10, 0.18) |

---

- **ES** = effect size
- **95% CI** = 95% confidence interval
- **I-squared** = percentage of total variation due to heterogeneity between studies
- **p** = statistical significance of effect size

**Note:** *I*² = heterogeneity between the groups; >=50% indicates statistically significant differences.
Heterogeneity between groups: p = 0.000

I-V Overall (I-squared = 66.5%, p = 0.000)

Poor vs. Moderate
Mean Difference: 0.03 (-0.03, 0.09)
I-V Subtotal (I-squared = 79.5%, p = 0.000)

Moderate vs. Increasing
Mean Difference: 0.03 (-0.01, 0.10)
I-V Subtotal (I-squared = 0.0%, p = 0.933)

Poor vs. Decreasing
Mean Difference: 0.02 (-0.01, 0.06)
I-V Subtotal (I-squared = 0.0%, p = 0.996)

Month 3

- Poor vs. Decreasing
  Mean Difference: 0.01 (-0.11, 0.13)
  Weight: 1.20
- Poor vs. Moderate
  Mean Difference: 0.03 (-0.03, 0.09)
  Weight: 4.14
- Poor vs. Increasing
  Mean Difference: 0.01 (-0.08, 0.10)
  Weight: 2.12
- Decreasing vs. Moderate
  Mean Difference: 0.02 (-0.07, 0.11)
  Weight: 2.17
- Decreasing vs. Increasing
  Mean Difference: 0.02 (-0.09, 0.13)
  Weight: 1.41
- Moderate vs. Increasing
  Mean Difference: 0.04 (-0.03, 0.11)
  Weight: 3.09

I-V Subtotal (I-squared = 0.0%, p = 0.996)
  Mean Difference: 0.02 (-0.01, 0.06)
  Weight: 14.14

Month 6

- Poor vs. Decreasing
  Mean Difference: 0.12 (-0.00, 0.24)
  Weight: 1.09
- Poor vs. Moderate
  Mean Difference: 0.23 (0.17, 0.29)
  Weight: 4.72
- Poor vs. Increasing
  Mean Difference: 0.13 (0.04, 0.22)
  Weight: 2.17
- Decreasing vs. Moderate
  Mean Difference: 0.11 (0.08, 0.15)
  Weight: 13.42
- Decreasing vs. Increasing
  Mean Difference: 0.01 (-0.06, 0.08)
  Weight: 3.36
- Moderate vs. Increasing
  Mean Difference: 0.10 (0.07, 0.13)
  Weight: 19.55

I-V Subtotal (I-squared = 79.5%, p = 0.000)
  Mean Difference: 0.11 (0.09, 0.13)
  Weight: 44.32

Month 9

- Poor vs. Decreasing
  Mean Difference: 0.06 (-0.05, 0.17)
  Weight: 1.33
- Poor vs. Moderate
  Mean Difference: 0.17 (0.12, 0.22)
  Weight: 5.64
- Poor vs. Increasing
  Mean Difference: 0.14 (0.06, 0.22)
  Weight: 2.57
- Decreasing vs. Moderate
  Mean Difference: 0.11 (0.06, 0.16)
  Weight: 5.85
- Decreasing vs. Increasing
  Mean Difference: 0.08 (-0.01, 0.17)
  Weight: 2.17
- Moderate vs. Increasing
  Mean Difference: 0.03 (-0.01, 0.07)
  Weight: 8.89

I-V Subtotal (I-squared = 72.5%, p = 0.003)
  Mean Difference: 0.09 (0.07, 0.12)
  Weight: 26.46

Month 12

- Poor vs. Decreasing
  Mean Difference: 0.10 (-0.06, 0.26)
  Weight: 0.68
- Poor vs. Moderate
  Mean Difference: 0.06 (-0.02, 0.14)
  Weight: 2.70
- Poor vs. Increasing
  Mean Difference: 0.02 (-0.09, 0.13)
  Weight: 1.29
- Decreasing vs. Moderate
  Mean Difference: 0.04 (-0.03, 0.11)
  Weight: 3.66
- Decreasing vs. Increasing
  Mean Difference: 0.08 (-0.01, 0.17)
  Weight: 1.86
- Moderate vs. Increasing
  Mean Difference: 0.04 (-0.02, 0.10)
  Weight: 4.89

I-V Subtotal (I-squared = 0.0%, p = 0.933)
  Mean Difference: 0.05 (0.02, 0.08)
  Weight: 15.08

Heterogeneity between groups: p = 0.000

I-V Overall (I-squared = 66.5%, p = 0.000)
  Mean Difference: 0.09 (0.07, 0.10)
  Weight: 100.00

D+L Overall
  Mean Difference: 0.08 (0.05, 0.10)

I^2 = heterogeneity between groups; >=50% indicates statistically significant differences

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Online Data Supplement

Longitudinal Patterns of Mexican and Puerto Rican Children’s Asthma Controller Medication Adherence and Acute Healthcare Utilization

Kimberly J. Arcoleo, PhD, MPH, Colleen McGovern, PhD, MPH, RN, Karenjot Kaur, BA, Jill S. Halterman, MD, MPH, Jennifer Mammen, PhD, NP-C, Hugh Crean, PhD, Deepa Rastogi, MBBS, MS, Jonathan M. Feldman, PhD

Supplemental Figure Legend

Figure E1A. Categorical Cross-Sectional Adherence by Ethnicity

Figure E1B. Categorical Cross-Sectional Adherence by Child Sex

Figure E2A. Categorical Cross-Sectional Adherence by Poverty Status

Figure E2B. Categorical Cross-Sectional Adherence by Season

Figure E3A. Longitudinal Latent Class Analysis for Acute Visits by Adherence Class

Figure E3B. Longitudinal Latent Class Analysis for ED Visits/Hospitalizations by Adherence Class
Figure E3A. Longitudinal Latent Class Analysis for Acute Visits by Adherence Class
Figure E3B. Longitudinal Latent Class Analysis for ED Visits & Hospitalizations by Adherence Class