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

Kimberly J. Arcoleo, PhD, MPH

School of Nursing

University of Rochester

Rochester, NY, USA

Kimberly_arcoleo@urmc.rochester.edu

Colleen McGovern, PhD, MPH, RN

School of Nursing

University of North Carolina – Chapel Hill

Chapel Hill, NC, USA

cmmcgovernrn@gmail.com

Karenjot Kaur, BA

Ferkauf Graduate School of Psychology

Yeshiva University

Bronx, NY, USA

kkaur1@mail.yu.edu

Jill S. Halterman, MD, MPH

Department of Pediatrics

School of Medicine & Dentistry

University of Rochester

Rochester, NY, USA

jill_halterman@urmc.rochester.edu

Jennifer Mammen, PhD, NP-C

School of Nursing

University of Rhode Island

Providence, RI, USA

Jmammen@uri.edu

Hugh Crean, PhD

School of Nursing

University of Rochester

Rochester, NY, USA

hugh_crean@URMC.Rochester.edu

Deepa Rastogi, MBBS, MS

Albert Einstein College of Medicine

Children's Hospital at Montefiore,

Bronx, NY

DRASTOGI@montefiore.org

Jonathan M. Feldman, PhD

Ferkauf Graduate School of Psychology

Yeshiva University

Department of Pediatrics

Albert Einstein College of Medicine

Children's Hospital at Montefiore

Bronx, NY, USA

jonathan.feldman@einstein.yu.edu

Contact 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.

Keywords: medication adherence, asthma, healthcare disparities

Funding: This work was supported by the National Center for Complementary & Alternative Medicine Health [1R01AT005216-01, 2009-2015]

Running Head: patterns of controller medication adherence

Word count: 3499

78 At A Glance Commentary:

79 Scientific Knowledge on the Subject: There is a paucity of data on children's patterns of
80 asthma controller medication adherence and variations in adherence, particularly in the
81 Latino sub-groups, which may help explain the asthma health disparities observed
82 between Mexican and Puerto Rican children.

83 What This Study Adds to the Field: This is the first study to show that unique ethnicity
84 *within* Latino populations may be associated with different levels of controller medication
85 non-adherence risk and the relationship of these patterns to acute healthcare utilization.
86 These results add to our emerging evidence on children's patterns of ICS medication
87 adherence and suggest a need for clinical monitoring of ICS medication use and
88 development of targeted interventions to address suboptimal treatment patterns.

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

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 and Measures

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.

Main Results

23%-32% 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) and "Poor" (*OR*=5.62) adherence compared to Mexican children. Females had significantly greater odds of "Decreasing" (*OR*=4.80) and "Poor" (*OR*=5.20) 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.

Word count: 350

Introduction

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)

154 medication initiation (21) among a sample of long term care patients (*n*=13,922). The
155 results identified periods of non-adherence alternating with periods of regular ICS use.
156 LaForest et al. (20) examined ICS adherence over 12 months among children and
157 adults selectively recruited for high initial adherence. The investigators noted
158 fragmented episodes of ICS use which typically lasted several months even though all
159 individuals were adherent at baseline (20). A better understanding of controller
160 medication adherence patterns in children will provide evidence needed to identify
161 individuals at highest risk for non-adherence and acute healthcare utilization and offer a
162 more intensive intervention while using less-intensive approaches for those at low risk
163 preventing waste of precious healthcare resources.

164

165 A literature review revealed no studies directly examining controller medication
166 adherence between Mexican and Puerto Rican children; thus these analyses fill a
167 critical gap in our knowledge and offer insights to factors leading to asthma health
168 disparities between these Latino sub-groups. The objectives of these secondary
169 analyses were to: 1) identify patterns of children's ICS medication adherence over a 12
170 month assessment period in a sample of Mexican and Puerto Rican children with
171 persistent asthma; 2) examine sociodemographic and seasonal predictors of adherence
172 patterns and; 3) investigate asthma-related acute healthcare utilization based on these
173 patterns. To the best of our knowledge, this was the first study to examine objectively
174 measured longitudinal patterns of ICS medication adherence in children, explore
175 heterogeneity in adherence patterns within a sample of Latino children, and link those
176 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 (7%-12%) with the largest proportion of children demonstrating poor adherence (23%-32%). Puerto Rican children had the highest proportion of poor adherence at each time period (63%-80%) compared to Mexican children (40%-49%)(Figure 2). 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% (Figure 3). Across all time periods, females demonstrated the highest proportions of poor adherence (55%-75%). At M3 and M6, more non-poor children demonstrated poor adherence compared to poor children. These differences dissipated over time (Figure 4). There were no seasonal differences in adherence at any time period (Figure 5). 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

313 increasing adherence (poor adherence shifting to moderate or good adherence) (15%)
314 (Figure 6). Table 2 presents the results for significant predictors of adherence class
315 membership; ethnicity, child sex, and poverty. No differences were observed for marital
316 status, caregiver's education, child's age, asthma duration, or number of family
317 members with asthma. Puerto Rican children had significantly higher odds of being in
318 the "Decreasing" and "Poor" adherence groups compared to Mexican children. Females
319 had significantly greater odds of being in the "Decreasing" and "Poor" adherence groups
320 compared to Males; no females were in the "Improving" adherence class. The
321 "Decreasing" adherence class was comprised of only poor children and these children
322 also had lower odds of being in the "Improving" adherence class. No interaction effects
323 of ethnicity with caregiver marital status, education, poverty, or child sex were observed
324 (data not shown).

325

326 Differences in asthma-related healthcare utilization (i.e., acute care visits and ED
327 visits/hospitalizations) were examined by adherence class and modeled by assessment
328 period across 12 months. Because of small class sizes and low frequency of healthcare
329 visits, we examined effect sizes to ascertain *clinically meaningful (*effect size >=.30)
330 differences between classes for acute care visits and ED visits/hospitalizations in
331 addition to *statistically significant* differences (Table 3). Figures 7 and 8 plot the mean
332 number of acute visits and ED visits/hospitalizations, respectively, at each assessment
333 period by adherence class. For acute visits, clinically meaningful differences were
334 observed between all adherence classes across all assessment periods except for M12
335 poor vs. moderate. 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. 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. 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. 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. 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. **O**ur 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: We want to thank the participating caregivers and children for their time and commitment to this study. We also thank our participating clinics and staff

for their ongoing collaboration as we continue to target children's asthma health disparities.

References

1. Guidelines for the diagnosis and management of asthma (EPR-3). 2012. Available from: https://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report.

2. Klok, T, Kaptein, A, Duiverman, EJ, Brand, PL. Long-term adherence to inhaled corticosteroids in children with asthma: Observational study. *Respiratory Medicine.* 2015;109(9):1114-1119.

3. McQuaid EL, Everhart, RS, Seifer, R, Kopel, SJ, Mitchell, DK, Klein, RB, Esteban, CA, Fritz GK, Canino G. Medication adherence among Latino and non-Latino white children with asthma. *Pediatrics.* 2012;129(6):1404-1410.

4. Akinbami, LJ, Simon, AE, Rossen, LM. Changing trends in asthma prevalence among children. *Pediatrics.* 2016;137(1):1-7.

5. Chan, AH, Stewart, AW, Harrison, J, Camargo, CA Jr, Black, PN, Mitchell, EA. The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: A randomised controlled trial. *The Lancet Respiratory Medicine.* 2015;3(3):210-219.

6. Osterberg, L, Blaschke, T. Adherence to medication. *New England Journal of Medicine.* 2005;353(5):487-497.

7. Keemink YS, Klok T, Brand PL. Long-term adherence to daily controller medication in children with asthma: The role of outpatient clinic visits. *Pediatr Pulmonol.* 2015 Nov;50(11):1060-4.

8. Engelkes, M, Janssens, HM, de Jongste, JC, Sturkenboom, MC,Verhamme, KM. Medication adherence and the risk of severe asthma exacerbations: A systematic review. *The European Respiratory Journal.* 2015;45(2):396-407.

9. Canino G, Koinis-Mitchell D, Ortega AN, McQuaid EL, Fritz GK, Alegria M. Asthma disparities in the prevalence, morbidity, and treatment of Latino children. *Soc Sci Med.* 2006 Dec;63(11):2926-37.

10. Sue S, Dhindsa MK. Ethnic and racial health disparities research: issues and problems. *Health Educ Behav.* 2006 Aug;33(4):459-69.

11. Hayes-Bautista DE. Research on culturally competent healthcare systems. Less sensitivity, more statistics. *Am J Prev Med.* 2003 Apr;24(3 Suppl):8-9.

12. Asthma Surveillance Data [Internet]. 2016 . Available from: https://www.cdc.gov/asthma/asthmadata.htm.

13. Rosser FJ, Forno E, Cooper PJ, Celedon JC. Asthma in Hispanics. An 8-year update. *Am J Respir Crit Care Med.* 2014 Jun 1;189(11):1316-27.

14. Lara M, Akinbami L, Flores G, Morgenstern H. Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. *Pediatrics.* 2006 Jan;117(1):43-53.

15. Choudhry S, Ung N, Avila PC, Ziv E, Nazario S, Casal J, et al. Pharmacogenetic differences in response to albuterol between Puerto Ricans and Mexicans with asthma. *American Journal of Respiratory & Critical Care Medicine.* 2005 Mar 15;171(6):563-70.

16. Sulaiman I, Seheult J, MacHale E, Boland F, O'Dwyer SM, Rapcan V, et al. A Method to Calculate Adherence to Inhaled Therapy that Reflects the Changes in Clinical Features of Asthma. *Ann Am Thorac Soc.* 2016 Nov;13(11):1894-1903.

17. Souverein PC, Koster ES, Colice G, van Ganse E, Chisholm A, Price D, et al. Inhaled Corticosteroid Adherence Patterns in a Longitudinal Asthma Cohort. *J Allergy Clin Immunol Pract.* 2017 Mar - Apr;5(2):448,456.e2.

18. Bidwal M, Lor K, Yu J, Ip E. Evaluation of asthma medication adherence rates and strategies to improve adherence in the underserved population at a Federally Qualified Health Center. *Res Social Adm Pharm.* 2017 Jul - Aug;13(4):759-66.

19. Blais L, Kettani FZ, Forget A, Beauchesne MF, Lemiere C, Ducharme FM. Assessing adherence to inhaled corticosteroids in asthma patients using an integrated measure based on primary and secondary adherence. *Eur J Clin Pharmacol.* 2017 Jan;73(1):91-7.

20. Laforest L, Belhassen M, Devouassoux G, Didier A, Ginoux M, Van Ganse E. Long-Term Inhaled Corticosteroid Adherence in Asthma Patients with Short-Term Adherence. *J Allergy Clin Immunol Pract.* 2016 Sep-Oct;4(5):890,899.e2.

21. Bernard V, De GS, Hughes DA, Kardas P, Jenny D, Todd R, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol.* 2012; 73(5):691-705.

22. Gore S, Aseltine RH,Jr, Colton ME. Social structure, life stress and depressive symptoms in a high school-aged population. *Journal of Health & Social Behavior.* 1992 Jun;33(2):97-113.

23. McQuaid EL, Kopel SJ, Klein RB, Fritz GK. Medication Adherence in Pediatric Asthma: Reasoning, Responsibility, and Behavior. *Journal of Pediatric Psychology.* 2003 July 01;28(5):323-33.

24. Schilling C, Atkins D, Edwards M. Are you targeting the right patients with your medication adherence programs? Eden Prairie, MN: OPTUM; 2015. Report No.: OPTPRJ8902 4/15.

25. Schreiber JB. Latent Class Analysis: An example for reporting results. *Res Social Adm Pharm.* 2017 Nov;13(6):1196-201.

26. Feldman BJ, Masyn KE, Conger RD. New approaches to studying problem behaviors: a comparison of methods for modeling longitudinal, categorical adolescent drinking data. *Dev Psychol.* 2009;45(3):652.

27. Arcoleo, K, Zayas, LE, Hawthorne, A, Begay R. Illness representations and cultural practices play a role in patient-centered care in childhood asthma: Experiences of Mexican mothers. *Journal of Asthma.* 2015;135(4):e965,-e973.

527 28. Conn KM, Halterman JS, Fisher SG, Yoos HL, Chin NP, Szilagyi PG. Parental
528 beliefs about medications and medication adherence among urban children with
529 asthma. *Ambul Pediatr.* 2005 Sep-Oct;5(5):306-10.

530 29. Feldman, JM, Steinberg, D, Kutner, H, Eisenberg, N, Hottinger, K, Sidora-Arcoleo,
531 K, Warman, K, Serebrisky, D. Perception of pulmonary function and asthma control:
532 The differential role of child versus caregiver anxiety and depression. *Journal of*
533 *Pediatric Psychology*. 2013;38(10):1091-1100.

534 30. Feldman JM, McQuaid EL, Klein RB, Kopel SJ, Nassau JH, Koinis-Mitchell D, et al.
535 Symptom perception and functional morbidity across a one-year follow-up in pediatric
536 asthma. *Pediatr Pulmonol*. 2007;42:339-347.

537 31. Koinis-Mitchell D, McQuaid EL, Seifer R, Kopel SJ, Nassau JH, Klein RB, Feldman
538 J, Wamboldt MZ,Fritz GK. Symptom perception in children with asthma: cognitive and
539 psychological factors. *Health Psychology*. 2009;28(2):226-37.

540 32. Fritz GK, McQuaid EL, Kopel SJ, Seifer R, Klein RB, Mitchell DK, et al. Ethnic
541 differences in perception of lung function: a factor in pediatric asthma disparities?. *Am J*
542 *Respir Crit Care Med.* 2010 Jul 1;182(1):12-8.

543 33. Kopel SJ, Walders-Abramson N, McQuaid EL, Seifer R, Koinis-Mitchell D, Klein RB,
544 et al. Asthma symptom perception and obesity in children. *Biological Psychology.* 2010
545 April 2010;84(1):135-41.

546 34. Yoos HL, Kitzman H, Henderson C, McMullen A, Sidora-Arcoleo K, Halterman JS,
547 et al. The impact of the parental illness representation on disease management in
548 childhood asthma. *Nursing Research.* 2007;56(3):167-74.

549 36. Naqvi M, Thyne S, Choudhry S, Tsai H, Navarro D, Castro R, et al. Ethnic-Specific
550 Differences in Bronchodilator Responsiveness Among African Americans, Puerto
551 Ricans, and Mexicans with Asthma. *Journal of Asthma.* 2007;44(8):639-648.

552 37. Moorman, JE, Akinbami, LJ, Bailey, CM, et al. National Surveillance of Asthma:
553 United States, 2001-2010. Washington, DC: Centers for Disease Control; 2012. Vital
554 Health Stat 3(35).

555 38. Kikidis D, Konstantinos V, Tzovaras D, Usmani OS. The Digital Asthma Patient: The
556 History and Future of Inhaler Based Health Monitoring Devices. *Journal of Aerosol*
557 *Medicine and Pulmonary Drug Delivery*. 2016;29(3):219-32.

558

559

560 Table 1. Sample Baseline Characteristics (*n*=123)

Variable	**Mexican (*N*=89) N (%)**	**Puerto Rican (*N*=34) N (%)**
Recruitment Site		
Hospital Clinic (NY)	17 (19.10)	34 (100)
Breathmobile (AZ)	61 (68.54)	0
School-based Health Center (AZ)	11 (12.36)	0
Season of Baseline Interview		
Summer	25 (28.09)	8 (23.53)
Fall	21 (23.60)	12 (35.29)
Winter	26 (29.21)	8 (23.53)
Spring	17 (19.10)	6 (17.65)
Child:	**N (%)**	**N (%)**
Child Sex (% Female)	31 (34.8)	15 (44.1)
Clinician-rated Asthma Severity		
Mild intermittent	9 (10.34)	3 (9.68)
Mild persistent	27 (31.03)	5 (16.13)
Moderate persistent	47 (54.02)	18 (58.06)
Severe persistent	4 (4.06)	5 (16.13)
Any Controller Medication Use in the Past Month (% Yes)	78 (87.64)	27 (79.41)
	Mean (SD)	**Mean (SD)**
Study Child's Age (Years)	9.53 (2.14)	8.64 (1.97)
Asthma Duration (# months since diagnosis)	68.28 (36.22)	82.21 (33.21)
% Adherent: Month 3	47.51 (30.05)	35.65 (28.91)
% Adherent: Month 6	53.47 (31.47)	35.44 (37.86)
% Adherent: Month 9	51.27 (28.68)	29.94 (27.57)
% Adherent: Month 12	53.09 (29.39)	26.41 (29.29)
Caregiver	**N (%)**	**N (%)**
Married (% Yes)	45 (50.56)	9 (26.47)
Poor (% Yes)	59 (66.29)	10 (29.41)
High School Graduate (% Yes)	34 (38.20)	19 (55.88)
Caregiver Sex (% Female)	85 (95.51)	32 (94.12)
	Mean (SD)	**Mean (SD)**
Caregiver's Age	34.57 (6.41)	36.00 (9.39)
# Family Members w/Asthma	1.17 (0.73)	0.82 (1.11)

561

562

563 Table 2. Sociodemographic Predictors of Controller Medication Adherence Class Membership

Variable	Model χ^2	Improving Adherence		Moderate Adherence		Decreasing Adherence		Poor Adherence	
		Prob (SE)	Odds Ratio	Prob (SE)	Odds Ratio	Prob (SE)	Odds Ratio	Prob (SE)	Odds Ratio
Ethnicity	9.15****								
Mexican		.90		.87		.70		.54	
Puerto		.10	.73	.13	REF	.30	2.86	.46	5.62
Rican		(.11)		(.07)		(.15)		(.09)	
Child Sex	85.07*								
Male		1.0		.78		.42		.40	
Female		0 (0)	0	.22	REF	.58	4.80	.60	5.20
				(.08)		(.19)		(.08)	
Poverty	99.49****								
Non-Poor		.63		.41		0		.49	
Poor		.38	.41	.59	REF	1.0 (0)	0	.51	.74
		(.15)		(.10)				(.08)	

564 * p<.05, **p<.0001

565 Prob=Probability

566 SE=Standard error

567

568 Table 3. Latent Class Membership and Healthcare Utilization by Time Period

	Acute Care Visits		ED Visits+Hospitalizations	
	Mean Difference (95% CI)	Cohen's *d*	Mean Difference (95% CI)	Cohen's *d*
Month 3				
Poor Adherence				
vs. Decreasing Adherence	0.07 (-.115, .255)	.32	0.01 (-.107, .127)	.07
vs. Moderate Adherence	0.23 (.139, .321)	1.13	0.03 (-.033, .093)	.20
vs. Increasing Adherence	0.15 (.020, .281)	.73	0.01 (-.078, .098)	.06
Decreasing Adherence				
vs. Moderate Adherence	0.30 (.218, .383)	2.35	0.02 (-.067, .107)	.18
vs. Increasing Adherence	0.22 (.116, .324)	1.67	0.02 (-.088, .128)	.16
Moderate Adherence				
vs. Increasing Adherence	0.08 (.021, .139)	.76	0.04 (-.033, .113)	.31
Month 6				
Poor Adherence				
vs. Decreasing Adherence	0.45 (-.107, 1.007)	.76	0.12 (-.003, .243)	.84
vs. Moderate Adherence	0.55 (.281, .819)	.93	0.23 (.173, .291)	1.80
vs. Increasing Adherence	0.36 (-.034, .754)	.60	0.13 (.043, .217)	.93
Decreasing Adherence				
vs. Moderate Adherence	0.10 (.017, .184)	.87	0.11 (.077, .147)	1.67
vs. Increasing Adherence	0.09 (-.047, .227)	.59	0.01 (-.060, .080)	.12
Moderate Adherence				
vs. Increasing Adherence	0.19 (.112, .268)	1.27	0.10 (.073, .131)	1.69
Month 9				
Poor Adherence				
vs. Decreasing Adherence	.012 (.011,.229)	.97	0.06 (-.051, .171)	.44
vs. Moderate Adherence	0.09 (.034, .146)	.71	0.17 (.116, .224)	1.41
vs. Increasing Adherence	0.02 (-.062, .102)	.14	0.14 (.060, .220)	1.05
Decreasing Adherence				
vs. Moderate Adherence	0.03 (-.029, .089)	.40	0.11 (.057, .163)	1.24
vs. Increasing Adherence	0.14 (.050, .230)	1.43	0.08 (-.007, .167)	.76
Moderate Adherence				
vs. Increasing Adherence	0.11 (.056, .164)	1.08	0.03 (-.013, .073)	.36
Month 12				
Poor Adherence				
vs. Decreasing Adherence	0.27 (.101, .439)	1.44	0.10 (-.056, .256)	.57
vs. Moderate Adherence	0.01 (-.089, .109)	.04	0.06 (-.018, .138)	.34
vs. Increasing Adherence	0.23 (.108, .352)	1.17	0.02 (-.093, .133)	.11
Decreasing Adherence				
vs. Moderate Adherence	0.26 (.108, .412)	1.55	0.04 (-.027, .107)	.44
vs. Increasing Adherence	0.04 (-.054, .134)	.38	0.08 (-.014, .174)	.75
Moderate Adherence				
vs. Increasing Adherence	0.22 (.109, .331)	1.24	0.04 (-.018, .098)	.38

569

570

571 Figure Legend

572 Figure 1. Categorical Cross-Sectional Adherence

573 Figure 2. Categorical Cross-Sectional Adherence by Ethnicity

574 Figure 3. Categorical Cross-Sectional Adherence by Child Sex

575 Figure 4. Categorical Cross-Sectional Adherence by Poverty Status

576 Figure 5. Categorical Cross-Sectional Adherence by Season

577 Figure 6. Longitudinal Latent Class Analysis: 4 Class Solution

578 Figure 7. Longitudinal Latent Class Analysis for Acute Visits by Adherence Class

579 Figure 8. Longitudinal Latent Class Analysis for ED Visits/Hospitalizations by
580 Adherence Class

581