

Association between Cumulative Syndromic Illness in the 1st Year of Life and Neurodevelopmental and Growth Outcomes among Infants in Rural Guatemala

Daniel Olson, Molly M. Lamb, Amy K. Connery, Desiree Bauer, M. Alejandra Paniagua-Avila, Kathryn L. Colborn, Alison Colbert, Muktha S. Natrajan, Jesse Waggoner, Evan J. Anderson, Mirella Calvimontes, Guillermo A. Bolaños, Stephanie Pettibone, Hana M. El Sahly, Flor M. Munoz*, Edwin J. Asturias*.
University of Colorado School of Medicine, Aurora, CO; Colorado School of Public Health, Aurora, CO; Emory University School of Medicine, Atlanta, GA; Center for Human Development, FUNSA LUD, Guatemala; The Emmes Corporation, Baylor College of Medicine, Houston, TX. *Study Co-Principal Investigators.

Background

- Guatemala has high rates (~48%) of childhood stunting and neurodevelopmental (ND) delay
- Chronic diarrhea is associated with stunting and ND delay (Scrimshaw et al, 1995)
- Recurrent respiratory/febrile illness likely also play a role but less well characterized
- We recently completed a longitudinal study (DMID 16-0057) to evaluate the ND outcomes following post-natal Zika virus infection among a cohort of 500 infants in rural Guatemala
- The study collected weekly syndromic illness data, allowing us to explore the association between self-reported illness and stunting/ND.

Objectives

- Evaluate the cumulative burden of parent-reported febrile, respiratory, and diarrheal illness among a cohort of infants living in rural Guatemala and the association with:
 - Stunting (height/age Z score)
 - Neurodevelopment (MSEL score)

Methods

- Infants (0-3 months old) were enrolled Jun 2017-Jul 2018 into a 12-month observational study
- Subjects were then visited weekly by study nurses and screened for the following parent-reported symptoms in the preceding week:
 - Fever, Cough, Vomiting/Diarrhea
- At 0, 6, and 12 months, infants were assessed for the following outcomes by trained psychologists:
 - Height-for age Z score
 - Mullen Scales of Early Learning (MSEL), Early Learning Composite (ECL) Score
- Multivariable logistic regression models were used to test associations between cumulative weeks of syndromic illnesses and the outcomes

- 425 infants completed the 12-month study
- Infants had illness for a median of 16 weeks; cough was most frequent (median: 11 weeks, range: 0-37 weeks), followed by diarrhea/vomiting (median 6 weeks: range: 0-27) and fever (median:3 weeks, range 0-16)

Table 1: Subject Characteristics and Association with Low Mullen Stage of Earning Learning (MSEL) Early Learning Composite (ELC) Score among Infants in Rural, SW Guatemala.

	MSEL > 85 [†] (n = 304)	MSEL ≤ 85 (n = 121)	p-value*
Age at enrollment, mo (SD)	1.26 (0.76)	1.46 (0.84)	0.02
Age at last visit, mo (SD)	13.05 (0.79)	13.31 (0.95)	0.007
Female sex, n (%)	158 (78)	44 (22)	0.004
Mother is literate, n (%)	285 (74)	102 (26)	0.002
Mom's education, n (%):			
None	14 (52)	13 (48)	
Primary school	168 (70)	71 (30)	0.007
Secondary school	96 (79)	29 (24)	
University/post-graduate	25 (83)	5 (17)	
Breastfeed (final visit), n (%)	210 (70)	91 (30)	0.10
Stunted (final visit), n (%)	94 (68)	45 (32)	0.21

[†]MSEL ECL score of 100 is the mean in the US, with standard deviation (SD) = 15 points. *t-test for continuous variables, and chi-square test or fisher's exact test for categorical variables

Table 2: Association between Frequency of Syndromic illness in the First Year of Life and Low MSEL ECL Score or Stunting at 12-15 Months.

Illnesses	MSEL ≤ 85 ^{*,†}		Stunted (-2 SD) ^{*,‡}	
	RR per week of illness (95% CI)	p-value	RR per week of illness (95% CI)	p-value
Total	1.01 (1.00-1.03)	0.14	1.0 (0.98-1.02)	0.97
Cough	1.02 (1.00-1.04)	0.048	1.0 (0.98-1.02)	0.97
Fever	1.06 (1.02-1.11)	0.005	0.97 (0.93-1.02)	0.30
Diarr/Vomit	0.99 (0.96-1.02)	0.65	1.0 (0.97-1.03)	0.98

*Adjusted for gender, breastfeeding at last visit, age at last visit, and mother's literacy. †MSEL Standard score is a dichotomous outcome modeled with a binomial distribution and a log link. ‡Stunted is a dichotomous outcome (height for age < 2 SD below the mean on WHO growth charts). Modeled with a binomial outcome and a log link.

Results

Figure 2. Geolocation and Cumulative Weeks of Syndromic Illness among Infants in the Trifinio Region of SW Guatemala, 2017-19.

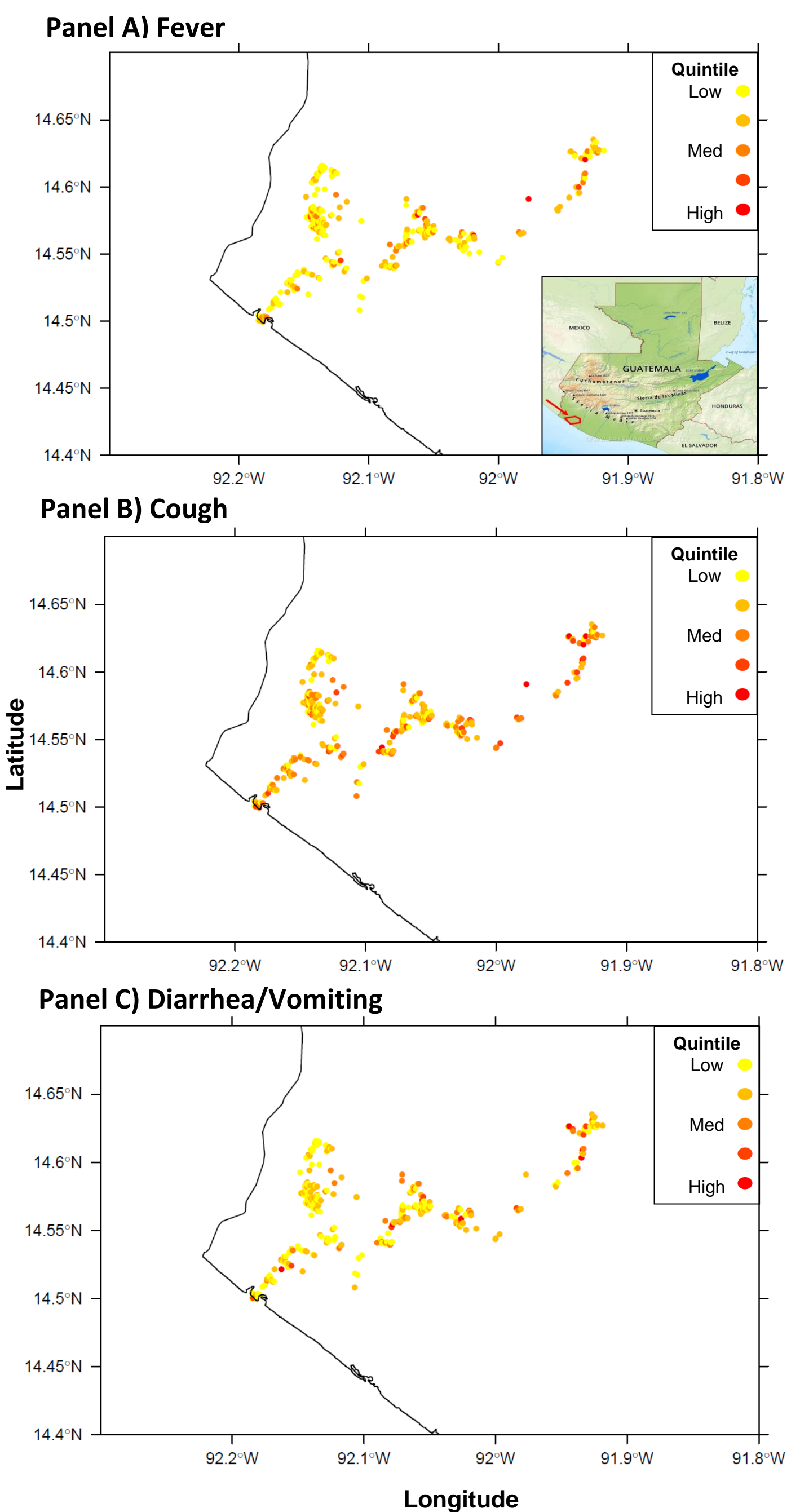
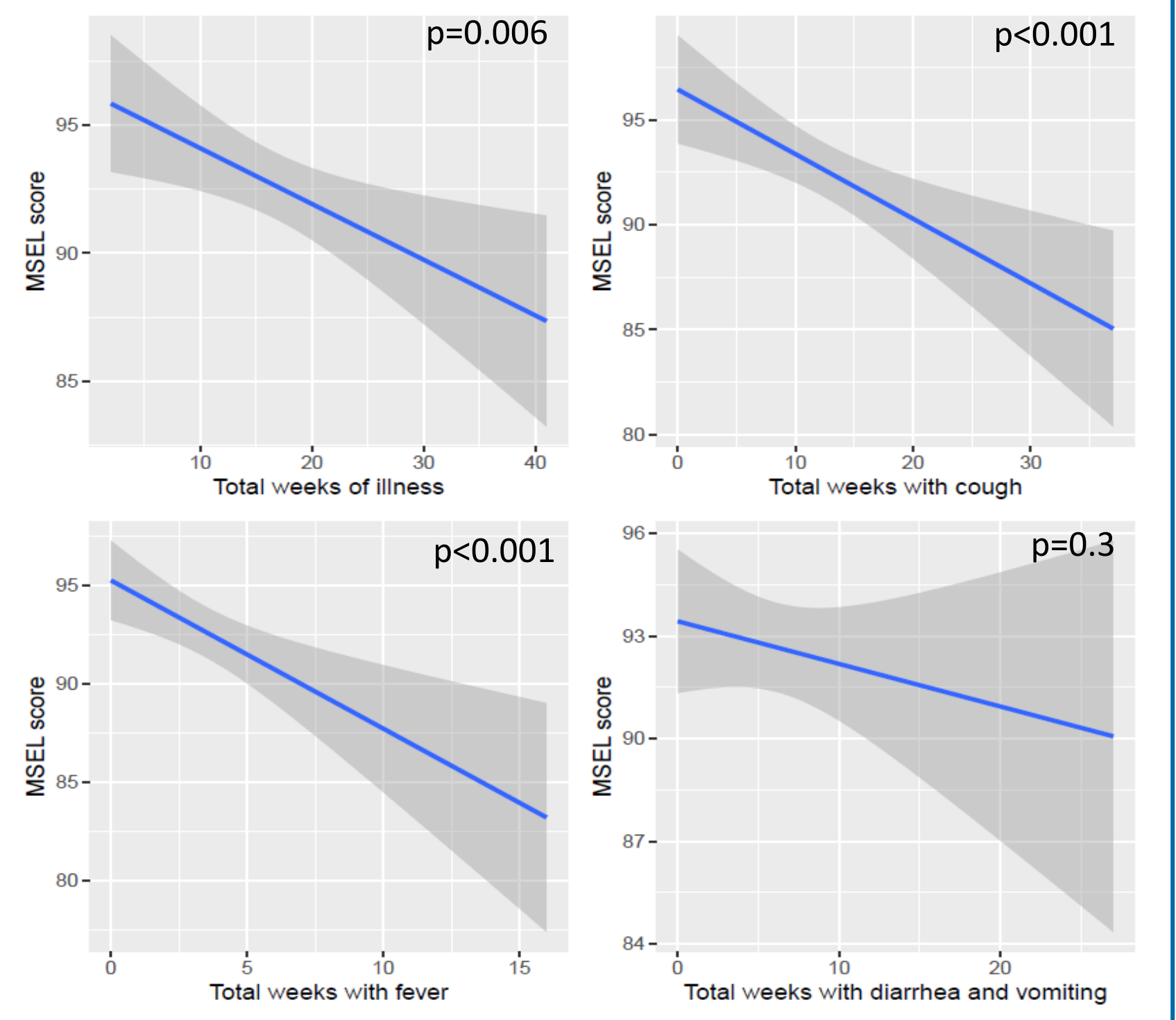


Figure 1. Cumulative Syndromic Illness and MSEL ECL Score (continuous) among Infants in Rural, SW Guatemala.



Conclusions

- In this rural, resource-limited region of Guatemala, recurrent febrile, respiratory and diarrheal illnesses were common among infants.
- Cumulative weeks of febrile and respiratory illnesses were associated with worse ND outcome at 12-15 months; there was not a significant association with diarrhea.
- Cumulative syndromic illnesses were not associated with stunting at 12-15 months.

Acknowledgements: Paola Arroyave, Sara Hernández, Maria Alejandra Martínez, Neudy Rojop, Edgar Barrios, Kareen Arias, Andrea Chacon, and the 16-0057 Study Team; Walla Dempsey, Kay Tomashak, Mary Smith Gail Tauscher, Wendy Keitel and the VTEU team; Andrea Holliday, Stephanie Pettibone, and the Emmes team
- DMID 16-0057: NIAID Contract HHSN2722013000151 Task Order HHSN27200013 (Co-PIs: FMM and EJA). Dr. Olson supported by K23AI143967 and CTSI Grant Number UL1 TR001082. **Contact:** Daniel.Olson@cuanschutz.edu