Machine Learning Identifies Key Risk Factors of Linear Growth Faltering and Death in Young Children With and Without Diarrhea

Sharia M. Ahmed[1], Benjamin Brintz[2], Patricia Pavlinac[3], James A. Platts-Mills[4], Karen L. Kotloff[5], Daniel T. Leung[1]

[1]Div of Infectious Disease, UofU School of Medicine, [2]Div of Epidemiology, U of U School of Medicine, [3]Dept of Global Health, University of Washington, [4]Div Of Infectious Diseases and Intl Health, University of Virginia, [5]Dept of Pediatrics, University of Maryland

Introduction

- Stunting: height-for-age (HAZ) z-score >2 standard deviations below population mean (1).
- ~140 million children stunted globally (2).
- Short-term: Stunting leads to worse health, delayed cognitive development, and increased expenses (medical care, lost work) (3).
- Long-term: Stunting contributes to adult comorbidities, including obesity, reproductive issues, reduced school performance, decreased work ability (3).
- The causes of stunting are multifaceted, including national, neighborhood, household, individual factors (4).
- 13.5% of all stunting is attributable to diarrheal disease (4).
- Seeking care for any cause (i.e. diarrhea) is an opportunity to identify children at risk for negative outcomes (e.g. growth faltering, death).
- **Aim: Use machine learning methods to identify key risk factors predictive of growth faltering and death for children with and without diarrhea in low and middle income countries (LMICs).**

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Sharia M Ahmed
Division of Infectious Diseases, University of Utah
sharia.m.ahmed@utah.edu

Predictive Models of Growth Faltering and Death

	0-11 months		12-23 months		24-59 months	
	Cases	**Control**	**Cases**	**Control**	**Cases**	**Control**
			Growth Faltering			
Number of outcome (%)	n=3068	n=4414	n=2494	n=3967	n=1773	n=3582
AUC (95% CI)	1027 (33%)	1299 (29%)	540 (22%)	549 (15%)	83 (5%)	31 (1%)
Top 10 Predictors	0.63 (0.62, 0.64)	0.71 (0.69, 0.73)	0.61 (0.60, 0.63)	0.67 (0.66, 0.69)	0.59 (0.58, 0.61)	[failed to converge]
	HAZ	HAZ	HAZ	HAZ	Respiratory rate	HAZ
	MUAC	Height	MUAC	Height	Temperature	MUAC
	Temperature	MUAC	Respiratory rate	MUAC	HAZ	Height
	Respiratory Rate	Wealth	Temperature	Respiratory rate	Age	Wealth
	Wealth	Respiratory rate	Wealth	Wealth	MUAC	Temperature
	Age	Temperature	Age	Age	Wealth	Age
	# ppl house	# ppl house	# ppl house	Temperature	# ppl house	# ppl house
	# share latrine	Age	Recomnd. ORS	# ppl house	# share latrine	# sleeping rms
	# diarrhea days	# sleeping rms	# sleeping rms	# sleeping rms	# sleeping rms	Respiratory rate
	# sleeping rms	# <5yr	Water source	# <5yr	Feces disposal	# <5yr
			Death			
Number of outcome (%)	n=3369	n=4556	n=2792	n=4110	n=1895	n=3665
AUC (95% CI)	98 (3%)	22 (<1%)	51/2792 (2%)	12 (<1%)	17 (1%)	3 (<1%)
Top 10 Predictors	0.79 (0.75, 0.83)	0.64 (0.55, 073)	0.82 (0.78, 0.88)	0.56 (0.45, 0.67)	0.84 (0.80, 0.87)	[failed to converge]
	MUAC	HAZ	MUAC	Height	MUAC	MUAC
	HAZ	Temperature	HAZ	HAZ	Arthritis	Arthritis
	Respiratory rate	Height	# ppl house	Temperature	HAZ	HAZ
	Convulsions	Respiratory rate	Temperature	Wealth	Flaky skin	Wealth
	Temperature	MUAC	Wealth	MUAC	Abn. Hair	Height
	Wealth	Wealth	Respiratory rate	Respiratory rate	Convulsions	Edema
	Age	Convulsions	Convulsions	Memory	Temperature	Previous diarr care
	# ppl house	Memory	# diarrhea days	# ppl house	Respiratory rate	Water
	Water source (enrollment & f-up)	# ppl house	Age	Convulsions	Family relationship	Temperature
		Age	Feces disposal	# sleeping rms	Age	Feces disposal

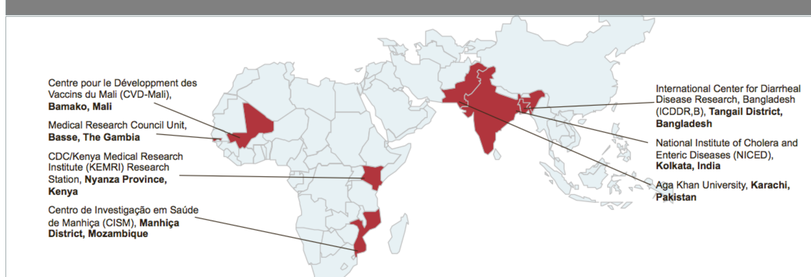
Results

- The youngest children (0-11 mo) experienced the most growth faltering and death.
- There were few deaths in controls, but growth faltering was prevalent in the youngest controls.
- Top predictors were similar for growth faltering and death across cases, controls, and age categories, and included child descriptors, individual symptoms, and household socio-economic status markers.
- Using this data, we had moderate discriminative ability to predict growth faltering in cases across all age groups (AUC ~ 0.6).
- Our models had lightly higher ability to predict growth faltering in controls (AUC ~ 0.7).
- There was good discriminative ability to predict death in cases (AUC ~ 0.8), but poor ability in controls.

Conclusions

- We were able to predict with moderate discriminative ability which children experienced growth faltering, especially in the youngest children.
  - Risk factors and predictive ability were the same for cases and controls.
  - **Any healthcare contact represents an opportunity to identify children most at risk of growth faltering.**
- We had good ability to predict child mortality when children sought care for acute diarrheal disease.
  - **When children present for acute diarrhea care, we can identify children most likely to die at the hospital and after discharge.**

Global Enteric Multicenter Study (GEMS)



Gates Foundation funded study of children's diarrhea conducted in 7 different countries (5)
Data collected 2007-2011 in children <5 years
Case-control study of children <60months seeking care for acute moderate or severe diarrhea
Acute diarrhea: 3+ looser than normal stools within 24 hours
Each case matched with 1-3 community controls without diarrhea
Clinical & epidemiological info collected from cases and controls at enrollment and ~60 days later
150+ possible predictors explored

Methods

Outcomes

- **Growth faltering:** decrease ≥0.5 height-for-age z-score (HAZ) over 60 days
- **Mortality**: any death between enrollment and 60 day follow-up

Predictive Model Building

- variable screening via random forest
  - rank variables based on reduction in variance
  - 5-fold cross-validation
- Fit regression models using:
  - Random forest regression
  - Logistic regression
- C-statistic (AUC) to assess predictive ability

$$\Delta \text{HAZ}\ (Y/N) = age + income + HH\ size + etc.$$
$$death\ (Y/N) = age + income + HH\ size + etc.$$

References

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