



# Development and Validation of the Asthma Burden Index

Herman Mitchell, PhD

Rho, Inc  
Chapel Hill

Inner City Asthma Consortium

National Institute of Allergy and Infectious Disease



# Introduction

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- Asthma symptoms as a primary outcome in intervention trials can be confounded by medication adjustments
- Not a problem if the study goal is to increase medication use, with the aim of decreasing symptoms
- However, if the goal is to reduce the overall burden of asthma by:
  - Reducing environmental exposures, or
  - Initiating immune-based therapies
- Then symptom measures alone will not capture the reduction in asthma burden

# Development of the Asthma Burden Index

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- Our goal was to develop a composite outcome that combines medication use with asthma risk and impairment measures
- Reduction in asthma burden could include:
  - ↓ symptoms and rescue med use
  - ↓ controller medication needed to maintain control
  - ↓ exacerbations and health care utilization
  - ↑ pulmonary function measurements

# Characteristics of the Asthma Burden Index

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In studies of medication treatment:

If symptoms go down, but medications go up – the ABI is likely to stay the same

In environmental intervention studies:

Both medications use and symptoms should be reduced, leading to a decrease in the ABI

In immunotherapy studies:

Both medications use and symptoms should be reduced, leading to a decrease in the ABI

# Asthma Burden Index Method for Development

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## Step 1:

Factor analysis to identify independent components and combine asthma outcome measures for all aspects of disease severity

## Step 2:

Gather a panel of asthma experts to provide scoring and weights for the various components of asthma severity

# Determining Unique Asthma Outcome Factors

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- Factor Analysis employed to:
  - Examine the independence of asthma outcomes
  - Determine the minimum number of factors to be measured

# Asthma Outcomes

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- Days of Symptoms
- Nights of Symptoms
- Days of Albuterol
- Nights of Albuterol
- Steroids Prescribed
- LABA Prescribed
- FEV1 % Predicted
- FEV1/FVC
- Prednisone Use
- Unscheduled Visits
- Hospitalizations

# Factor Analysis of Asthma Outcomes

Asthma Outcomes	Asthma Components	% of Variance
Days of Symptoms	Symptoms	23%
Nights of Symptoms		
Days of Albuterol		
Nights of Albuterol		
Steroids Prescribed	Treatment	16%
LABA Prescribed		
FEV1 % Predicted	Lung Function Measures	15%
FEV1/FVC		
Prednisone Usage	Prednisone and UV	12%
Unscheduled Visits		
Hospitalizations	Hospitalizations	10%

# Weighting the Asthma Outcomes measures

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Employed a modified Delphi technique to reach consensus among a panel of experts in order to weight and score each factor and its components

# Delphi Consensus Method

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1. Experts provide individual responses to a facilitator
2. Responses are shared anonymously among the expert group, along with comments
3. Experts discuss the initial round results
4. Experts provide second round of individual responses
5. These are again anonymously shared for a discussion to reach consensus

# Delphi Consensus Method

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In this case, the experts provided weights for the importance of asthma factors associated with:

1. Controller Medication Use
2. Spirometry (FEV1% predicted or personal best)
3. Daytime Symptoms and/or Albuterol Use
4. Nighttime Symptoms and/or Albuterol Use
5. Unscheduled Visits, Prednisone Use, Hospitalizations

# Weighting Process - example

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- Sample question:
  - Please distribute 100 points among these 4 variables based upon their relative importance to overall asthma burden:
    - Days of Symptoms in the last 2 weeks
    - Days of Albuterol use in the last 2 weeks
    - Nights of Symptoms in the last 2 weeks
    - Nights of Albuterol use in the last 2 weeks

# Weighting Process for ABI Components and Factors

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- 26 ICAC investigators participated in a web-based survey
  - (1) Ranking of factor importance by distributing 100 points across each component of that factor
  - (2) Assignment of comparative factor burden by distributing weights across each of the five factors
- 7 survey respondents met to reach a consensus interpretation of results

# Asthma Burden Index Factors Rankings

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<b>Factors</b>	<b>Weight</b>
Utilization	30%
Treatment	25%
Day Symptoms	15%
Night Symptoms	15%
Lung Function	15%

# Asthma Burden Index

## Sample ABI Calculations

ABI Component Scores								
Health Care Utilization		Unscheduled Visit		Prednisone		Hospitalization		
Points of Burden		8		9		24		
Treatment		Albuterol prn	Low-Dose ICS	Low-Dose ICS + LABA or Medium-Dose ICS		Medium- Dose ICS	High-Dose ICS	
Points of Burden		0	5	10		15	20	
Days of Symptoms		0-3		4-9		10-13		14
Points of Burden		0		5		10		15
Nights of Symptoms		0-1		2		3-4		5-14
Points of Burden		0		4		8		14
Lung Function Measurements		>85%		80-84%		70-79%		<70%
Points of Burden		0		4		8		15

# Asthma Burden Index

## Sample ABI Calculations

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- Patient 1
  - One Emergency Department Visit
  - One Prednisone Burst
  - High Dose of ICS

# Asthma Burden Index

## Sample ABI Calculations

	Utilization	Treatment	Day Sym	Night Sym	Lung Function	ABI
Participant 1	17	20	0	0	0	37

ABI Component Scores			
Health Care Utilization	Unscheduled Visit	Prednisone	Hospitalization
Points of Burden	8	9	24

Treatment	Albuterol prn	Low-Dose ICS	Low-Dose ICS + LABA or Medium-Dose ICS	Medium-Dose ICS	High-Dose ICS
Points of Burden	0	5	10	15	20

Days of Symptoms	0-3	4-9	10-13	14
Points of Burden	0	5	10	15

Nights of Symptoms	0-1	2	3-4	5-14
Points of Burden	0	4	8	14

Lung Function Measurement	>85%	80-84%	70-79%	<70%
Points of Burden	0	4	8	15

# Asthma Burden Index

## Sample ABI Calculations

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- Patient 2
  - No urgent care visits or prednisone
  - Low dose of ICS
  - 14 days of symptoms in past 2 weeks
  - 3 nights of symptoms
  - FEV<sub>1</sub> 75% of predicted

# Asthma Burden Index

## Sample ABI Calculations

	Utilization	Treatment	Day Sym	Night Sym	Lung Function	ABI
Participant 2	0	5	15	8	8	36

ABI Component Scores			
Health Care Utilization	Unscheduled Visit	Prednisone	Hospitalization
Points of Burden	8	9	24

Treatment	Albuterol prn	Low-Dose ICS	Low-Dose ICS + LABA or Medium-Dose ICS	Medium-Dose ICS	High-Dose ICS
Points of Burden	0	5	10	15	20

Days of Symptoms	0-3	4-9	10-13	14
Points of Burden	0	5	10	15

Nights of Symptoms	0-1	2	3-4	5-14
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# Asthma Burden Index

## Sample ABI Calculations

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Participant 2	0	5	15	8	8	36

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Lung Function Measurement	>85%	80-84%	70-79%	<70%
Points of Burden	0	4	8	15

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# ABI Statistical Characteristics

# ABI is more Stable than ACT<sup>®</sup> or MSD



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Outcome Measure	Cross-Visit Correlation*	Cronbach's Alpha
ABI	0.53	0.38
ACT <sup>®</sup>	0.26	0.72
Symptom Days per 2 Weeks	0.12	0.83

\* Also known as Interclass Correlation Coefficient (ICC)

# ABI is more Stable than ACT<sup>®</sup> or MSD

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# Conclusion

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The Asthma Burden Index is an innovative composite approach to combining components of a complex disease into a single and intuitive outcome

# Acknowledgements

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- The ACE Trial participants and their families
- Co-authors J.J. Wildfire, C. Sorkness, W. Morgan, and the Inner-City Asthma Consortium Investigators
- Funded by NIAID, NIH (N01-AI-25496, HHSN272200900052C and N01-AI-25482)

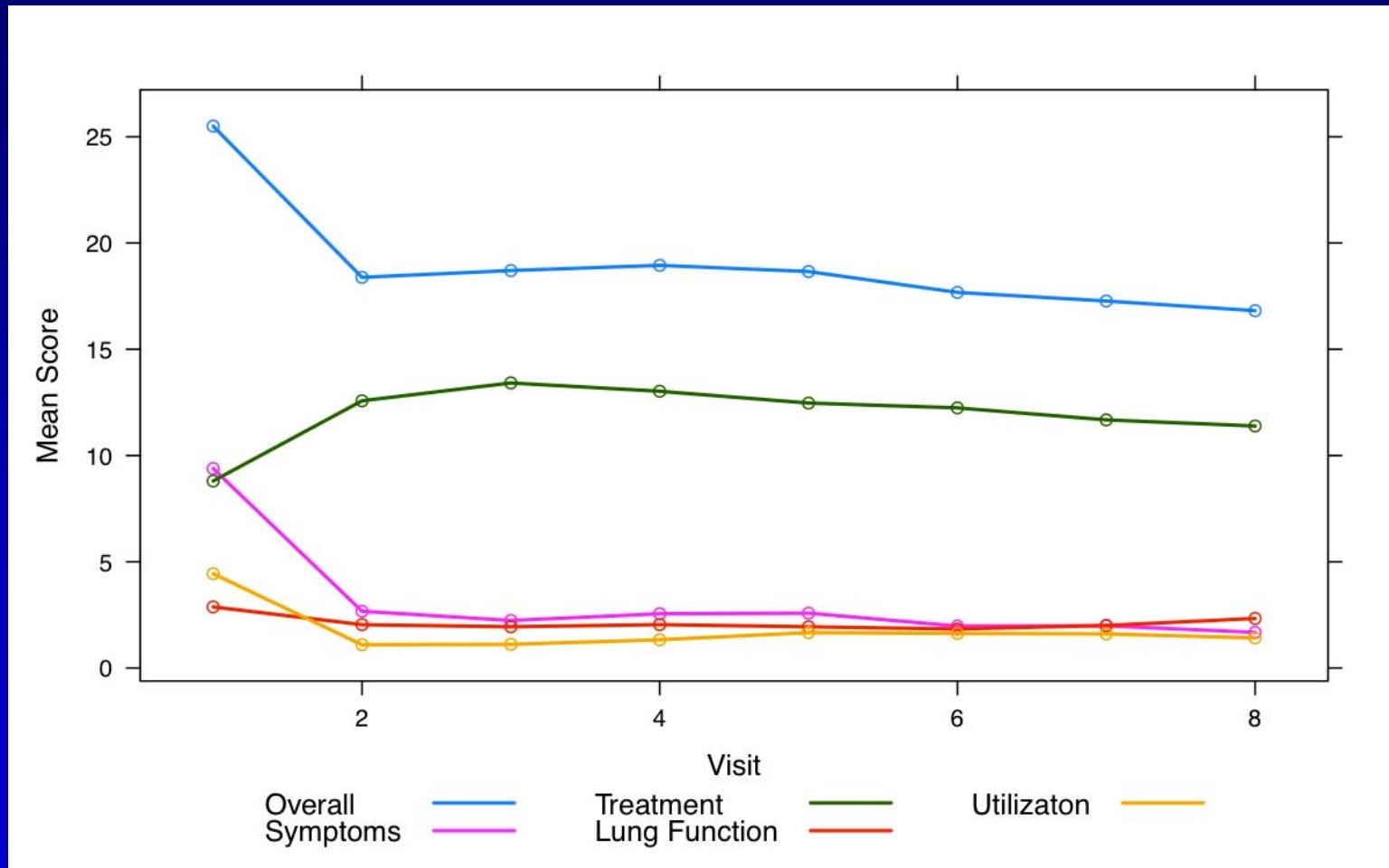
# Reserve Slides

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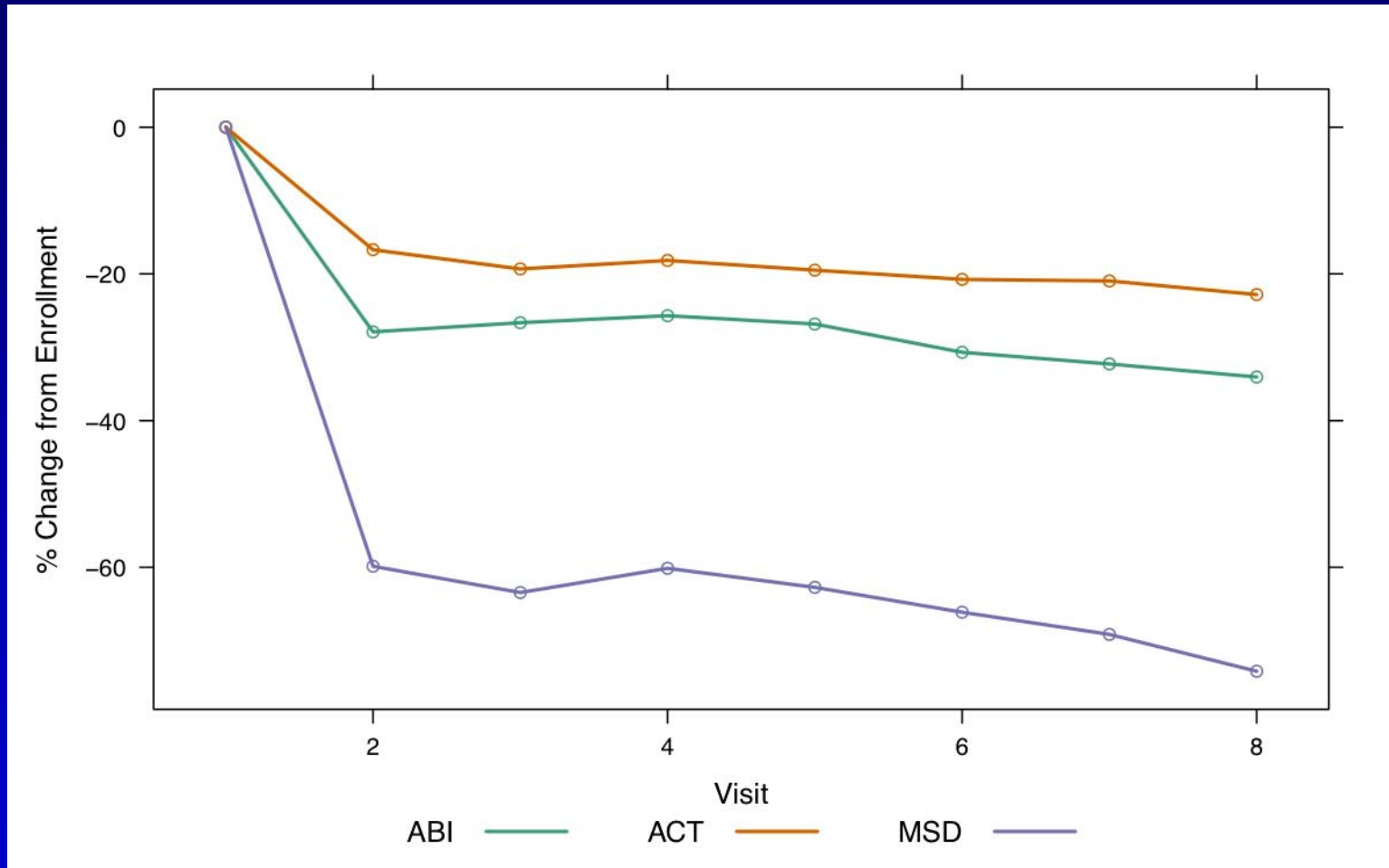
# Factor Analysis Results

Factor	% of Variance										
Symptoms		23%									
Treatment					16%						
Lung Function Measures							15%				
Prednisone and UV									12%		
Hospitalizations										10%	
<b>Asthma Components</b>	Days of Symptoms	Nights of Symptoms	Days of Albuterol	Nights of Albuterol	Steroids Prescribed	LABA Prescribed	FEV1 % Predicted	FEV1/FVC	Prednisone Usage	Unscheduled Visits	Hospitalizations

# ABI Distribution in ACE



# % Change in ACE Outcomes



ACT<sup>®</sup> = Asthma Control Test

MSD = Maximum symptom days / 2 weeks

# ABI Distribution in ACE

ACE Visit		Total ABI	Component Scores: Mean (% of ABI)				
			Day Sx	Night Sx	Lung Fx	Tx	HCU
Enrollment	1	25.5	4.3 (17)	5.1 (20)	2.9 (11)	8.8 (35)	4.4 (17)
Randomization	2	18.4	1.5 (8)	1.2 (7)	2.0 (11)	12.6 (68)	1.2 (7)
Double Blind	3-8	18.1	1.2 (7)	1.0 (6)	2.0 (11)	12.4 (69)	1.5 (8)
Max. Possible		105	15 (14)	14 (13)	15 (14)	20 (19)	41 (39)

ACE = Asthma Control Evaluation trial

# ABI is Correlated with Other ACE Outcomes

ACE Visit		CORRELATIONS		
		ABI vs ACT <sup>®</sup>	ABI vs MSD	MSD vs ACT <sup>®</sup>
Enrollment	1	- 0.44	0.48	- 0.61
Randomization	2	- 0.37	0.46	- 0.55
Double Blind	3	- 0.34	0.47	- 0.59
	4	- 0.47	0.50	- 0.60
	5	- 0.46	0.55	- 0.64
	6	- 0.39	0.46	- 0.61
	7	- 0.48	0.45	- 0.68
	8	- 0.47	0.47	- 0.64

ACT<sup>®</sup> = Asthma Control Test  
MSD = Maximum symptom days / 2 weeks

# Summary of Validation Results

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- ABI Validation
  - Moderate correlations with other Sx measures in ACE
    - MSD  $r = 0.46, p < 0.01$
    - ACT<sup>®</sup>  $r = -0.37, p < 0.01$
  - While significant, these are lower than correlation between ACT<sup>®</sup> & MSD ( $r = -0.55$ ), as expected
- Cronbach's Alpha 0.38 at ACE baseline
  - Lower than standard cut-off of 0.70 due to wide-ranging ABI components
- Cross visit ICC of ABI (0.53,  $p = 0.02$ ) > than MSD (0.12,  $< 0.05$ ) and ACT<sup>®</sup> (0.26,  $< 0.05$ )
  - Confirms stability of ABI across visits