

# **Are Crohn's Parents More Risk Averse Than Adult Patients?**

## **Acceptable Tradeoffs between Efficacy and Adverse-Event Risks**

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# Background

- n Patients with Crohn's disease (CD) are willing to accept the risk of serious adverse event (SAE) for specified therapeutic benefits\*
- n Parents' willingness to accept tradeoffs for their children may be different than adults
- n Objective:  
Compare the maximum acceptable risk (MAR) of SAEs of the parents of children with CD and adult CD patients

\* Sands et al., Crohn's Disease Patients Willingness to Accept the Risks of Serious Adverse Events in Exchange for Clinical Benefits. DDW, Los Angeles, May 24, 2006



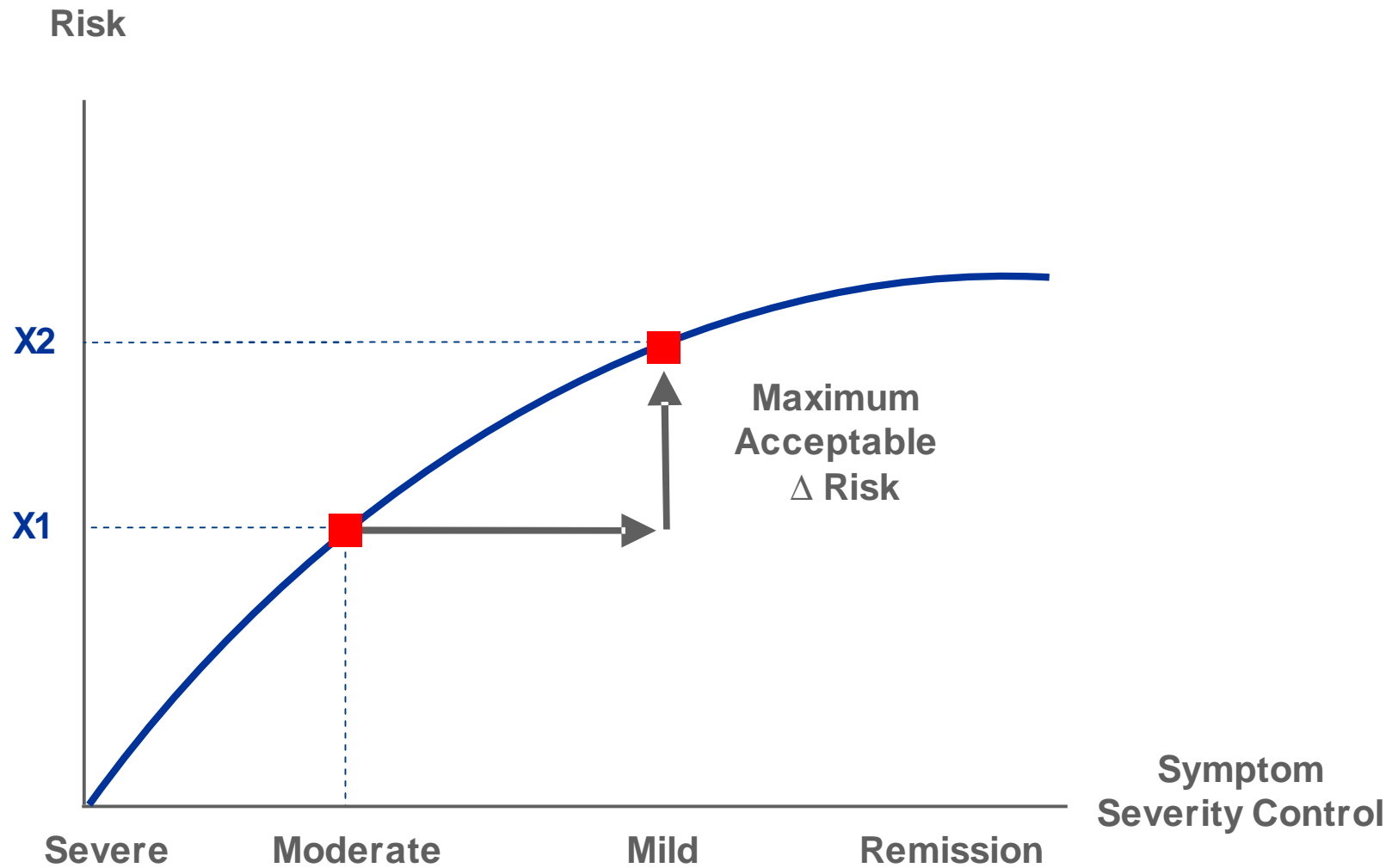
# Conjoint Analysis (CA) Method

- n **Extensively tested for validity and reliability in**
  - § market research
  - § transportation economics
  - § environmental economics
  
- n **Permits estimating trade-offs among attributes, including both time and money**
  
- n **Uses question formats that resemble clinical decisions**

# Which treatment would you choose if these were the only options?

Treatment Feature	Treatment A	Treatment B
Severity of Crohn's symptoms	<p>Moderate:</p> <ul style="list-style-type: none"> <li>▫ Moderate pain most days or severe pain on some days</li> <li>▫ About 8 or more diarrhea stools per day</li> <li>▫ Generally feel very poorly</li> <li>▫ Considerable problems with work and leisure activities</li> </ul>	<p>Remission:</p> <ul style="list-style-type: none"> <li>▫ No pain most days</li> <li>▫ No more than 1 diarrhea stool per day</li> <li>▫ Generally feel well</li> <li>▫ No problems with work or leisure activities</li> </ul>
Effect on serious complication	Prevents all of the serious complications	
Time between flare-ups	2 years	6 months
Treatment requires taking oral steroids	No	Yes
Chance of dying from a serious infection within 10 years	50 patients out of 1,000 (5%) will die	None would die
Chance of dying or severe disability from PML within 10 years	None would die or have severe disability	20 patients out of 1,000 (2%) will die or have severe disability
Chance of dying from lymphoma within 10 years	None would die	

# Risk-Benefit Tradeoff Curve





# Crohn's Disease

- n **CD is a chronic, recurring inflammatory disorder of the gastrointestinal tract.**
- n **CD affects men and women equally and affects as many as five in every 100,000 people in North America (CCFA, 2001)**
- n **Early symptoms: Abdominal pain, diarrhea, bleeding and weight loss, joint pain, fever, and fatigue.**
- n **Serious symptoms: Fistulas, abscesses, severe abdominal pain, persistent fatigue and weight loss, bowel obstruction, heightened risk of colon cancer.**

# Features of Conjoint Study

- n **7 attributes**
  - § 4 efficacy
  - § 3 risks
- n **Two versions**
  - § Patient's survey
  - § Parent's survey
- n **HealthTalk web panel**
- n **Benefit-risk trade-off tasks**
  - § 10 questions, 6 versions
    - 4 4 questions for internal validity tests
    - 4 Remaining 6 questions randomized
- n **Random-parameters choice model**

# TREATMENT ATTRIBUTES

ATTRIBUTES	LEVELS
Severity of symptoms	§ Remission § Mild § Moderate § Severe
Serious complications	§ Prevents all § Reduces some § Has no effect
Time between flare-ups	§ 6 months § 2 years
Need to take oral steroids	§ Yes § No
<u>10-year mortality risks</u> Serious infection PML Lymphoma	§ 0% § 0.5% § 2% § 5%

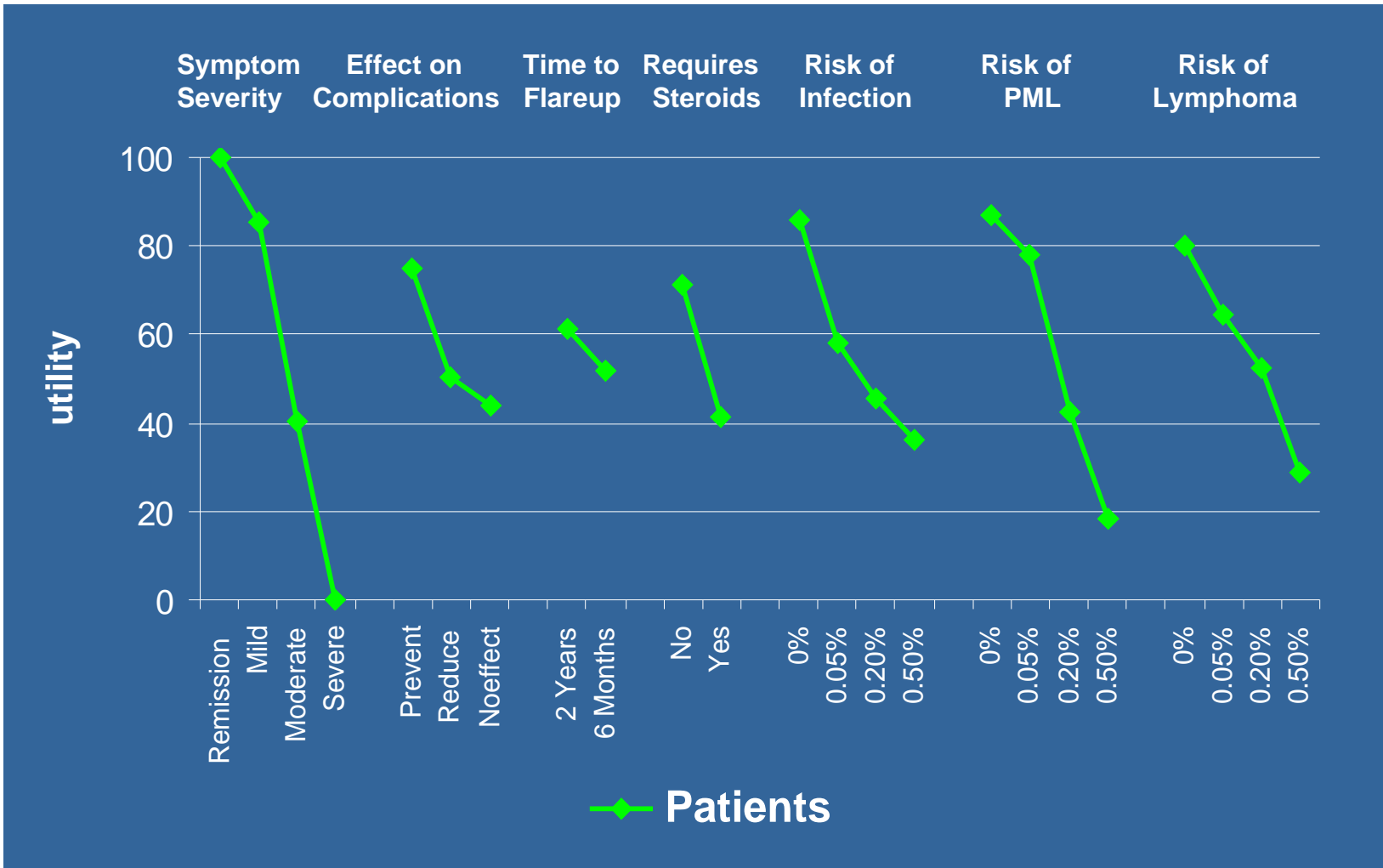
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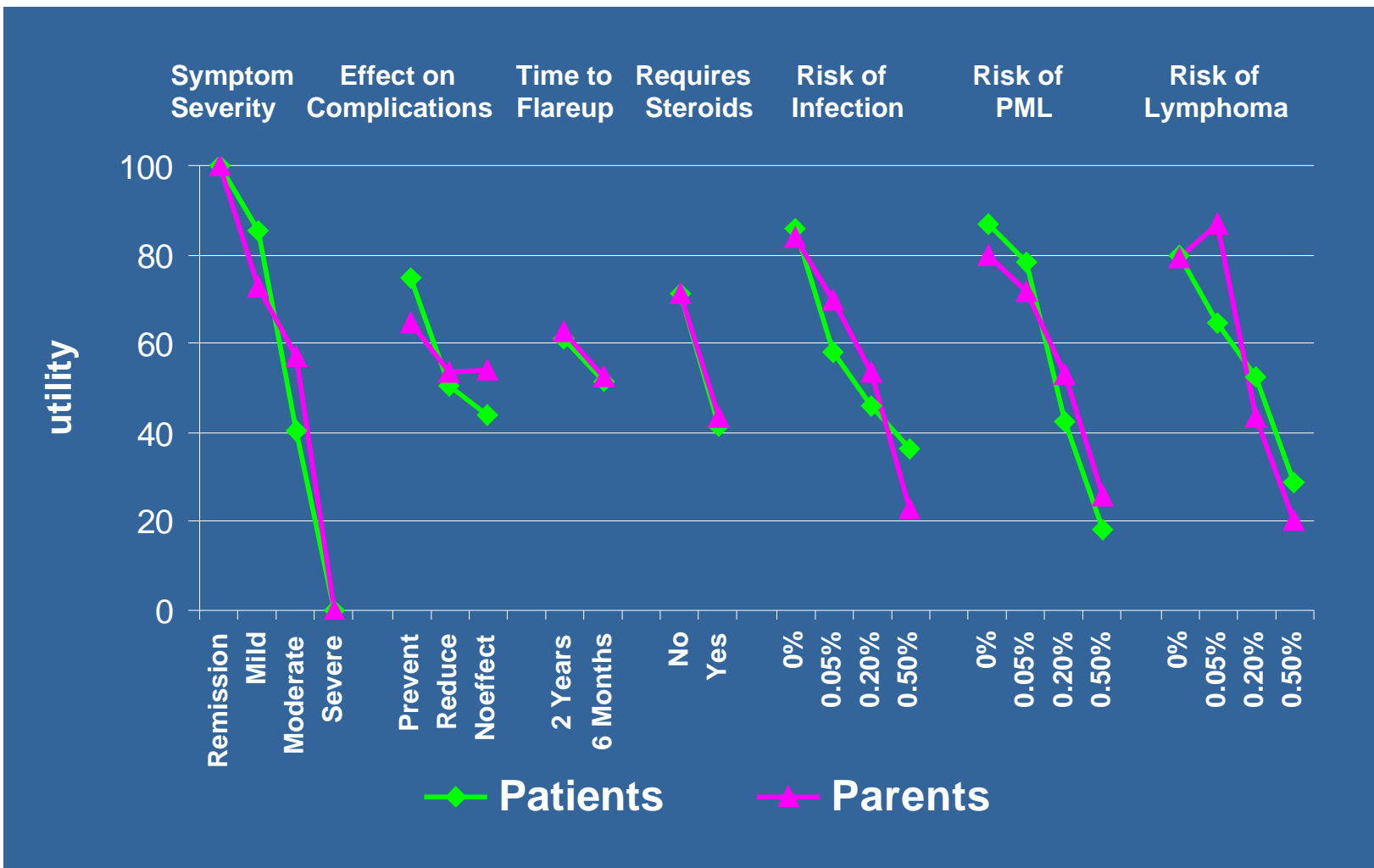
# Personal Characteristics

	Patients (n=580)	Parents (n=105)
<b>Mean Years since diagnosis (SD)</b>	<b>7.3 (3.2)</b>	<b>3.3 (2.2)</b>
<b>Effect of symptoms on daily life (%)</b>		
No problems	39	58
Some problems	45	32
Considerable problems	12	9
Unable to engage in activities	4	1
<b>Quite to extremely worried about PML (%)</b>	<b>38</b>	<b>69</b>
<b>Quite to extremely worried about Serious Infection (%)</b>	<b>25</b>	<b>61</b>
<b>Quite to extremely worried about Lymphoma (%)</b>	<b>32</b>	<b>69</b>

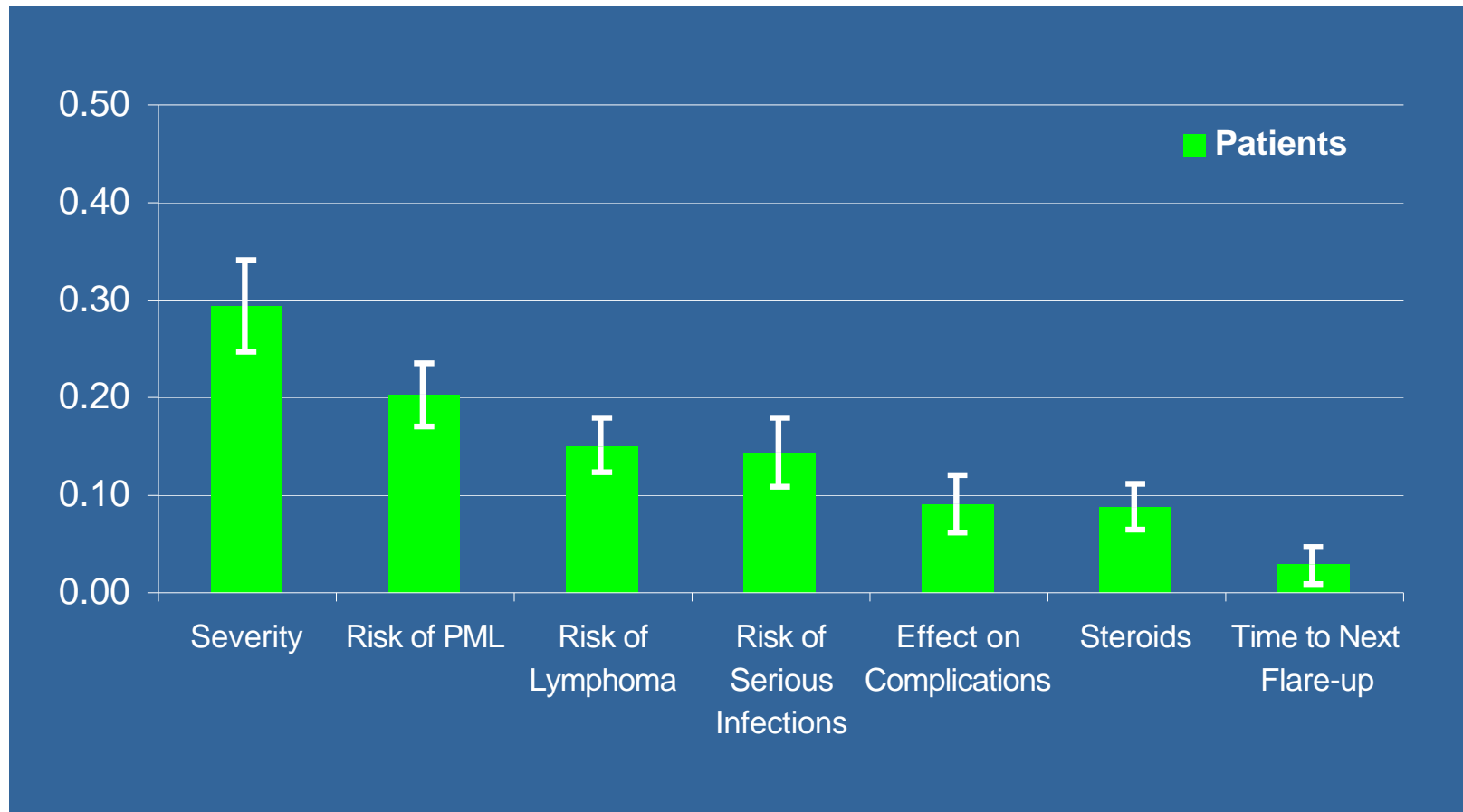
# Scaled Coefficients



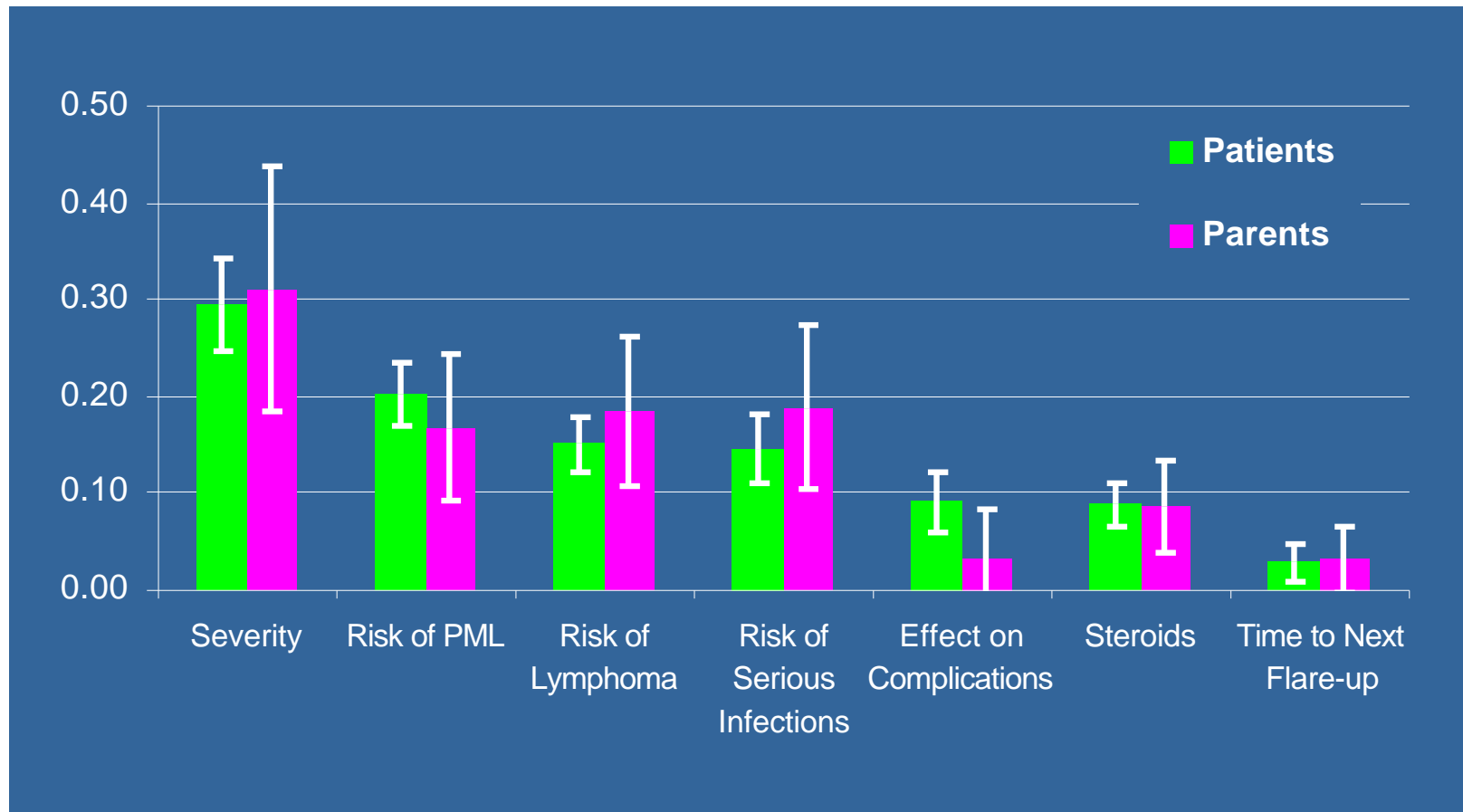
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# Relative Importance of Treatment Attributes



# Relative Importance of Treatment Attributes



# Maximum Acceptable Annual Risk

Benefit	PML		Serious Infection		Lymphoma	
	<i>Patients</i>	<i>Parents</i>	<i>Patients</i>	<i>Parents</i>	<i>Patients</i>	<i>Parents</i>
Severe to Moderate	0.18% (0.09-0.28)		0.22% (0.05-0.53)		0.36% (0.19-0.52)	
Moderate to Remission	0.39% (0.25-0.52)		0.55% (0.43-0.63)		0.55% (0.46-0.67)	
Severe to Remission	0.69% (0.55-0.83)		0.73% (0.64-0.87)		0.81% (0.68-1.05)	

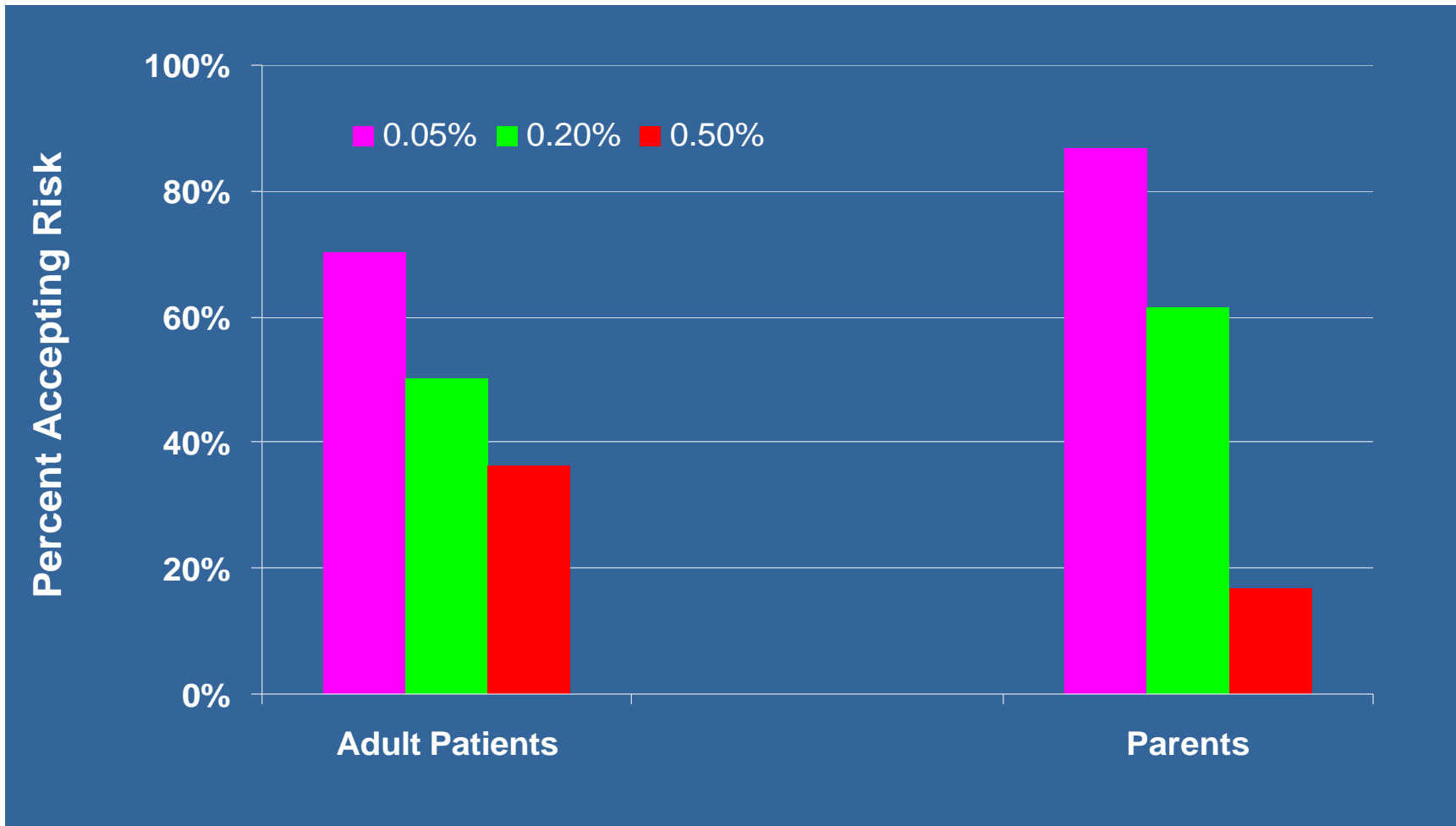
# Maximum Acceptable Annual Risk

Benefit	PML		Serious Infection		Lymphoma	
	<i>Patients</i>	<i>Parents</i>	<i>Patients</i>	<i>Parents</i>	<i>Patients</i>	<i>Parents</i>
Severe to Moderate		0.52% (0.10-1.14)		0.46% (0.08-0.91)		0.47% (0.15-1.20)
Moderate to Remission		0.38% (0.15-0.65)		0.32% (0.13-0.54)		0.29% (0.16-0.53)
Severe to Remission		0.87% (0.59-2.18)		0.74% (0.52-1.66)		1.05% (0.58-2.68)

# Maximum Acceptable Annual Risk

Benefit	PML		Serious Infection		Lymphoma	
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# Predicted Percent Accepting Annual PML Risk (moderate versus mild CD)





# Discussion



- n **Both types of respondents are willing to accept risk for significant therapeutic benefits.**
- n **MAR estimates are internally consistent and have face validity.**
- n **Parents value efficacy levels differently than patients.**
  - § Parent's MARs are driven by desire to keep their child from experiencing a severe CD state
- n **Risk tolerance:**
  - § Patients: PML < Infection < Lymphoma
  - § Parents: Infection ~ Lymphoma ~ PML



# Internal Validity Tests



- n **Stability test**
- n **Rational choice test**
- n **Monotonicity test**
- n **Transitivity test**

# Validity Test Results

Validity Test	Number of Failures per Patient	Percent of Respondents	
		Patients (%)	Parents (%)
<i>Stability</i>	0	92	90
	1	8	10
	>1	0	0
<i>Irrational Choice</i>	0	94	97
	1	6	3
	>1	0	0
<i>Monotonicity</i>	0	92	95
	1	4	4
	>1	4	1
<i>Transitivity</i>	0	92	94
	1	8	6

# Stability Violation

Task #1:

CATEGORY	DRUG A	DRUG B
Cost	\$4 per day	\$0.25 per day
Dosage	One pill once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?

Prefer Drug A

Prefer Drug B

Task #10:

CATEGORY	DRUG A	DRUG B
Cost	\$4 per day	\$0.25 per day
Dosage	One pill once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?

Prefer Drug A

Prefer Drug B

# Monotonicity Violation

Task #1:

CATEGORY	DRUG A	DRUG B
Cost	\$4 per day	\$0.25 per day
Dosage	One pill once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?

Prefer Drug A

Prefer Drug B

Task #4:

CATEGORY	DRUG A	DRUG B
Cost	\$2 per day	\$0.25 per day
Dosage	One pill once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?

Prefer Drug A

Prefer Drug B

# Rational-Choice Violation

CATEGORY	DRUG A	DRUG B
Cost	\$4 per day	\$0.25 per day
Dosage	Two pills twice a day	One pill once a day
Side effects	Moderate	Minor

Which drug do you prefer?

Prefer Drug A

Prefer Drug B

# Transitivity Violation

CATEGORY	DRUG A	DRUG B
Cost	\$4 per day	\$0.25 per day
Dosage	One pill once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?  Prefer Drug A  Prefer Drug B

CATEGORY	DRUG C	DRUG B
Cost	\$2 per day	\$0.25 per day
Dosage	Two pills once a day	Two pills twice a day
Side effects	Moderate	Minor

Which drug do you prefer?  Prefer Drug C  Prefer Drug B

CATEGORY	DRUG A	DRUG C
Cost	\$4 per day	\$2 per day
Dosage	One pill once a day	Two pills once a day
Side effects	Moderate	Moderate

Which drug do you prefer?  Prefer Drug A  Prefer Drug C



# Challenges of CA Approach

- n **Hypothetical choices do not have the same clinical, emotional, and financial consequences as real choices**
- n **Cognitively challenging for subjects**
- n **Requires expertise in**
  - § Qualitative and quantitative survey methods
  - § Experimental design
  - § Advanced statistical analysis

# Percent Accepting Risk

