RTI(h)(s)™ RTI HEALTH SOLUTIONS®

PATIENT AND PHYSICIAN BENEFIT-RISK PREFERENCES: EVIDENCE FROM 7 STUDIES

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RTI-HS Benefit-Risk Preference Studies

Therapeutic Area	Status
MS and Crohn's disease (Natalizumab)	6 publications
Vasomotor symptoms	J Women's Health, 2007
HIV	AIDS Patient Care and STDs, 2009
Platelet disorder (ITP)	Annals of Pharmacotherapy, provisional acceptance
Alzheimer's disease	AD and Associated Disorders, 2009
Irritable bowel syndrome	Value in Health, provisional acceptance
Kidney transplant	Completed
Renal cell carcinoma	Completed
Osteoarthritis	Data analysis
Statins case study (PhRMA/Next Steps)	Data collection
Triptans case study (PhRMA/Next Steps)	Data collection
Hepatitis B	Survey development
Psoriasis	Survey development
Hepatitis C	Survey development

Natalizumab Publications

Study	Publication
1. Crohn's disease patients	Gastroenterology, 2007
2. Adult Crohn's disease patients and parents of juvenile patients	Risk Analysis, 2009
3. Multiple sclerosis patients	Journal of Neurology, 2009
4. Patients, parents, and gastroenterologists	Journal of Managed Care Pharmacy, provisional acceptance
5. Implications for regulatory decision making	International Journal of Medical & Biological Frontiers, 2009
6. Theoretical derivation of MARs under non-linear risk preferences (methods)	Medical Decision Making, provisional acceptance

Natalizumab (Tysabri®) background

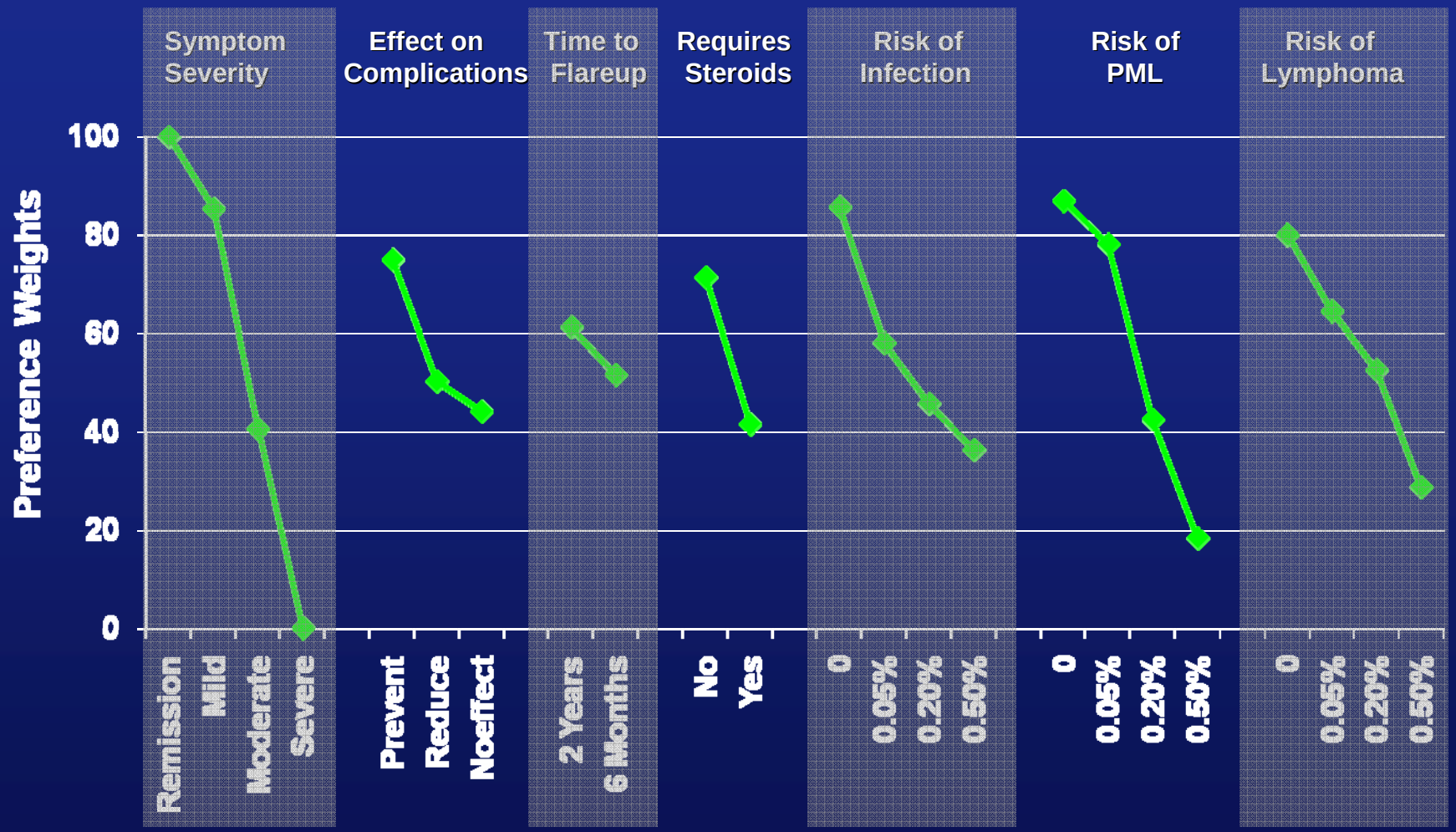
- **FDA approved 2004 for multiple sclerosis**
- **Withdrawn 2005 after 3 cases of progressive multifocal leukoencephalopathy (PML)**
- **Re-approved in 2006 with restrictions**
- **Approved in 2007 for Crohn's disease in US only**
- **Patient benefit-risk preference studies submitted to MS and Crohn's advisory committees**
- **24 PML cases to date (out of about 60,000)**

Features of Natalizumab Studies

- **Four versions**
  - MS patients
  - Adult Crohn's patients
    - Patient-support website (N=342)
    - Medical centers (natalizumab N=98; non-natalizumab N=130)
  - Parents of Crohn's children (N=105)
  - Gastroenterologists
- **Survey design**
  - Tradeoffs between efficacy and 3 mortality risks
  - 6 blocks of 10 questions
  - 4 questions for internal validity tests
- **Random-parameters choice models**

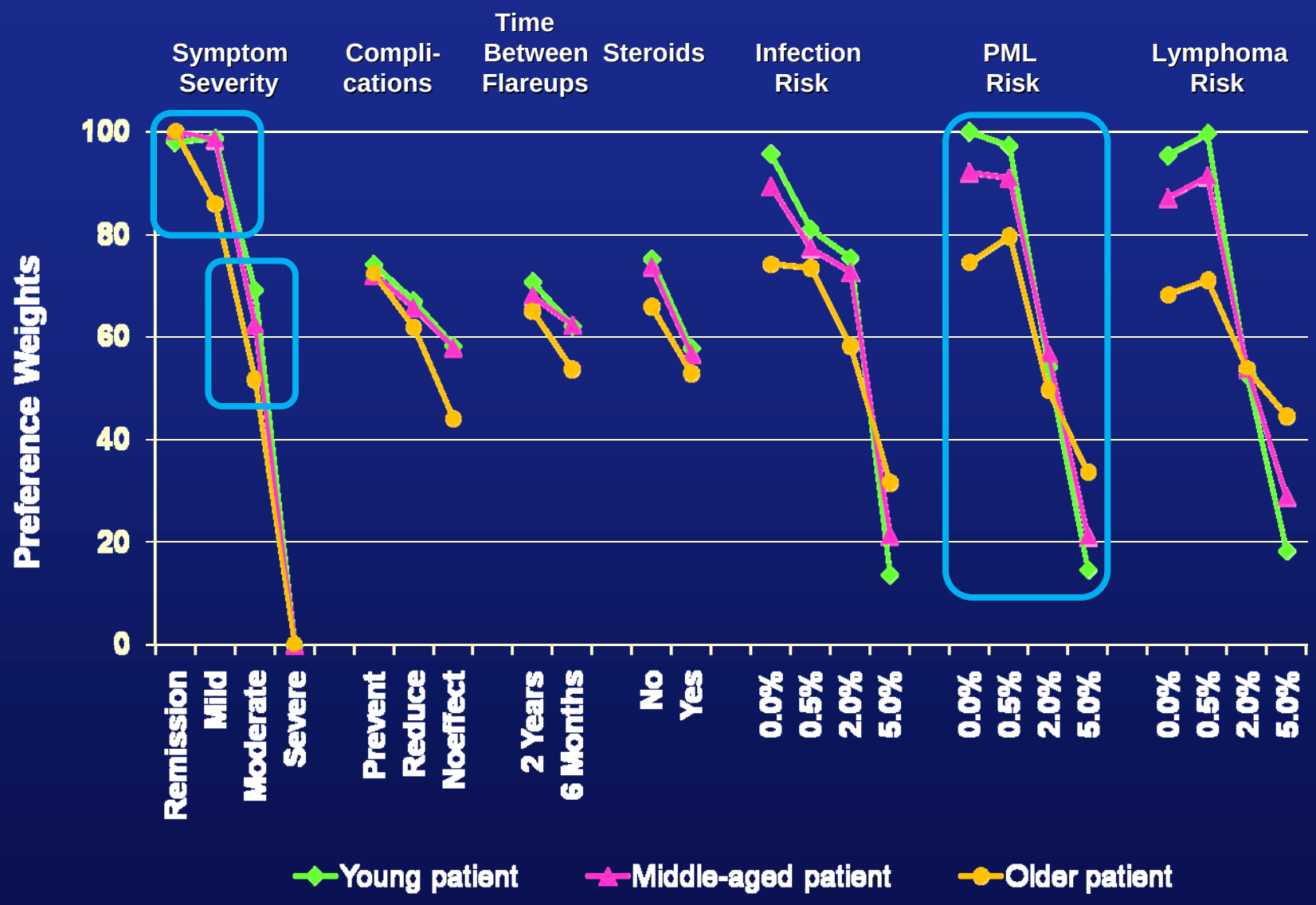
Crohn's Disease

Preference Estimates



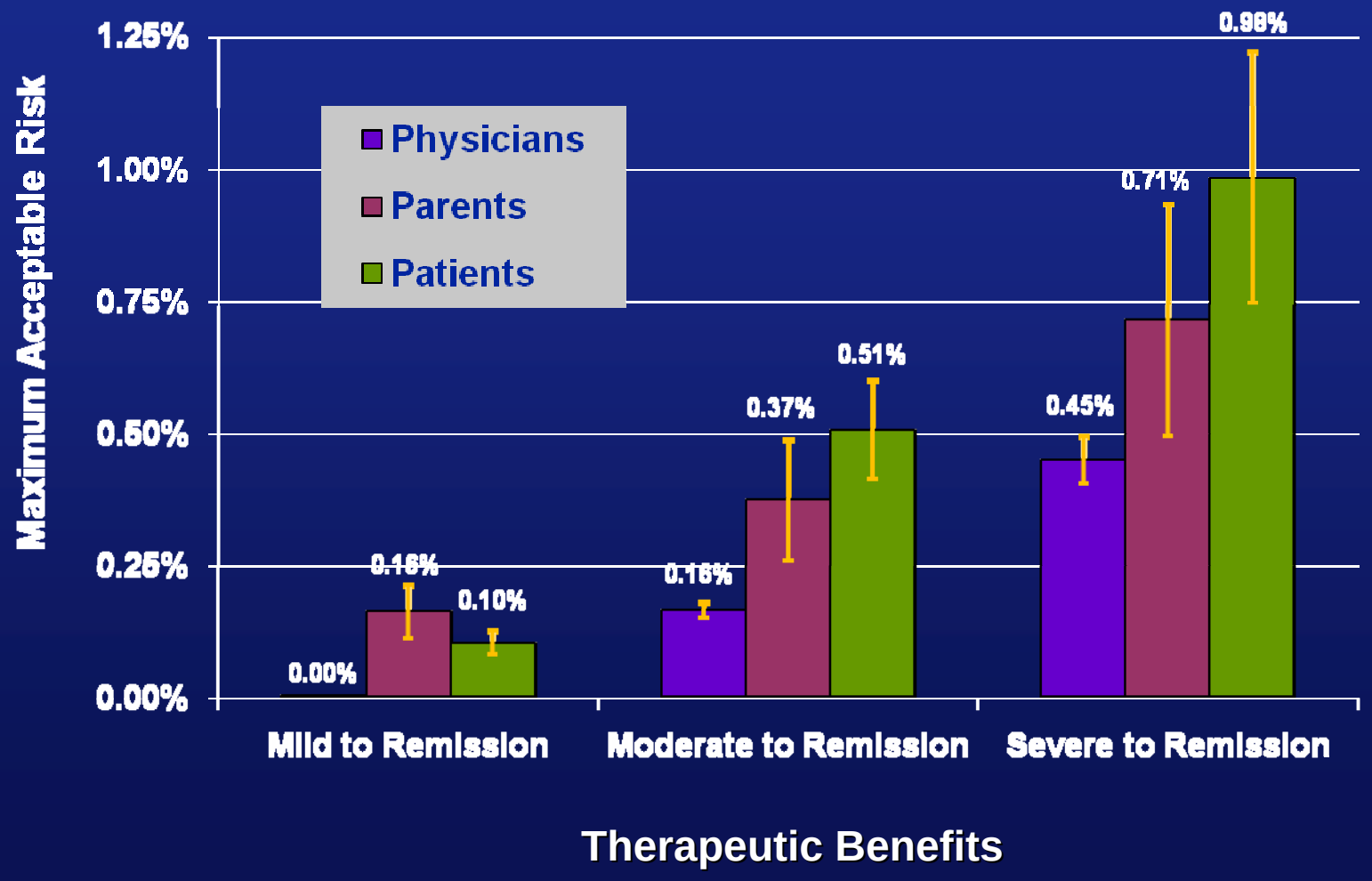
Crohn's Disease

Physician Preference Estimates by Patient Type



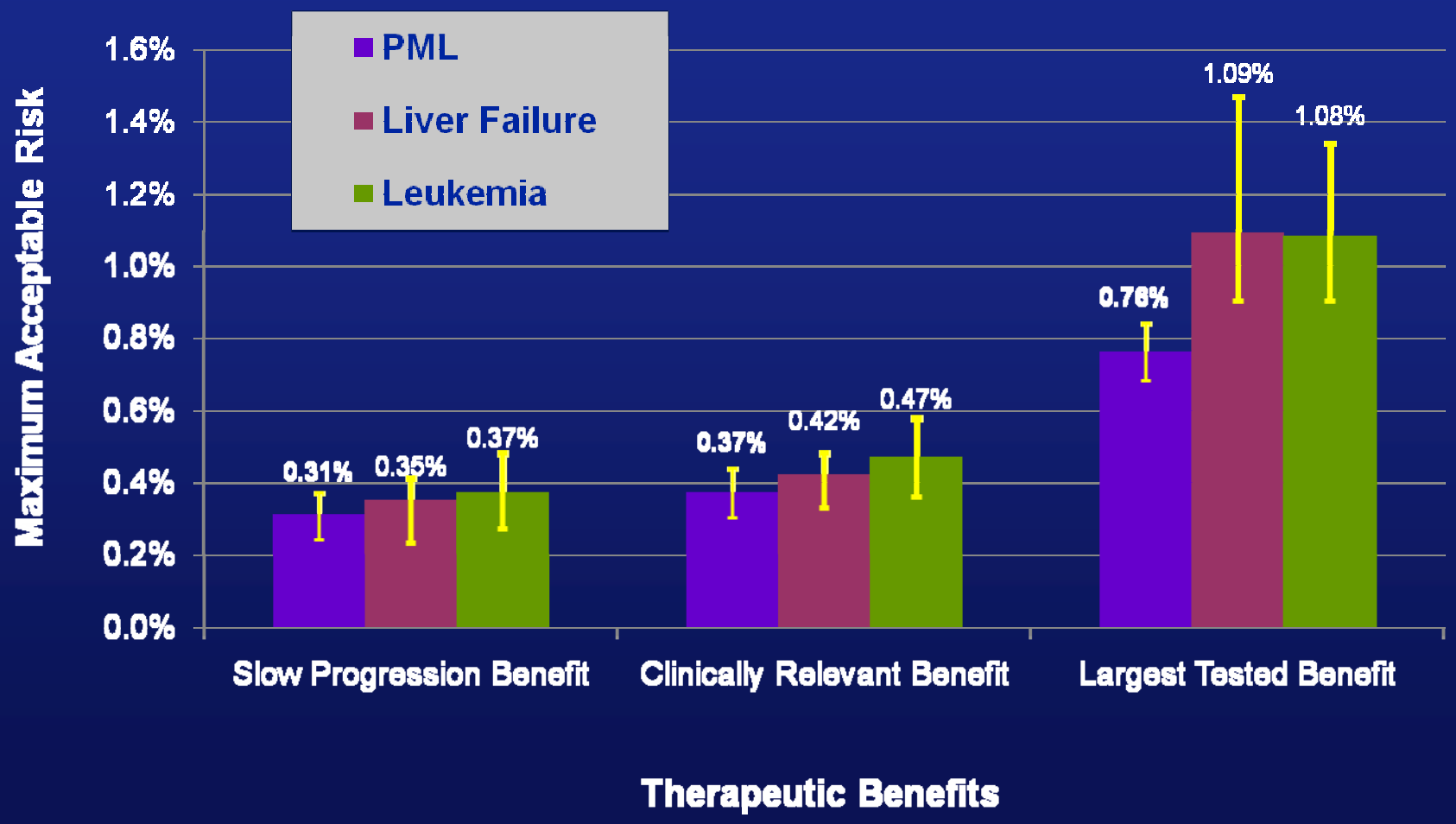
Crohn's Disease

Maximum Acceptable PML Risk



Multiple Sclerosis

Maximum Acceptable Risk



Vasomotor symptoms

Choice Task (Relative Risk Version)

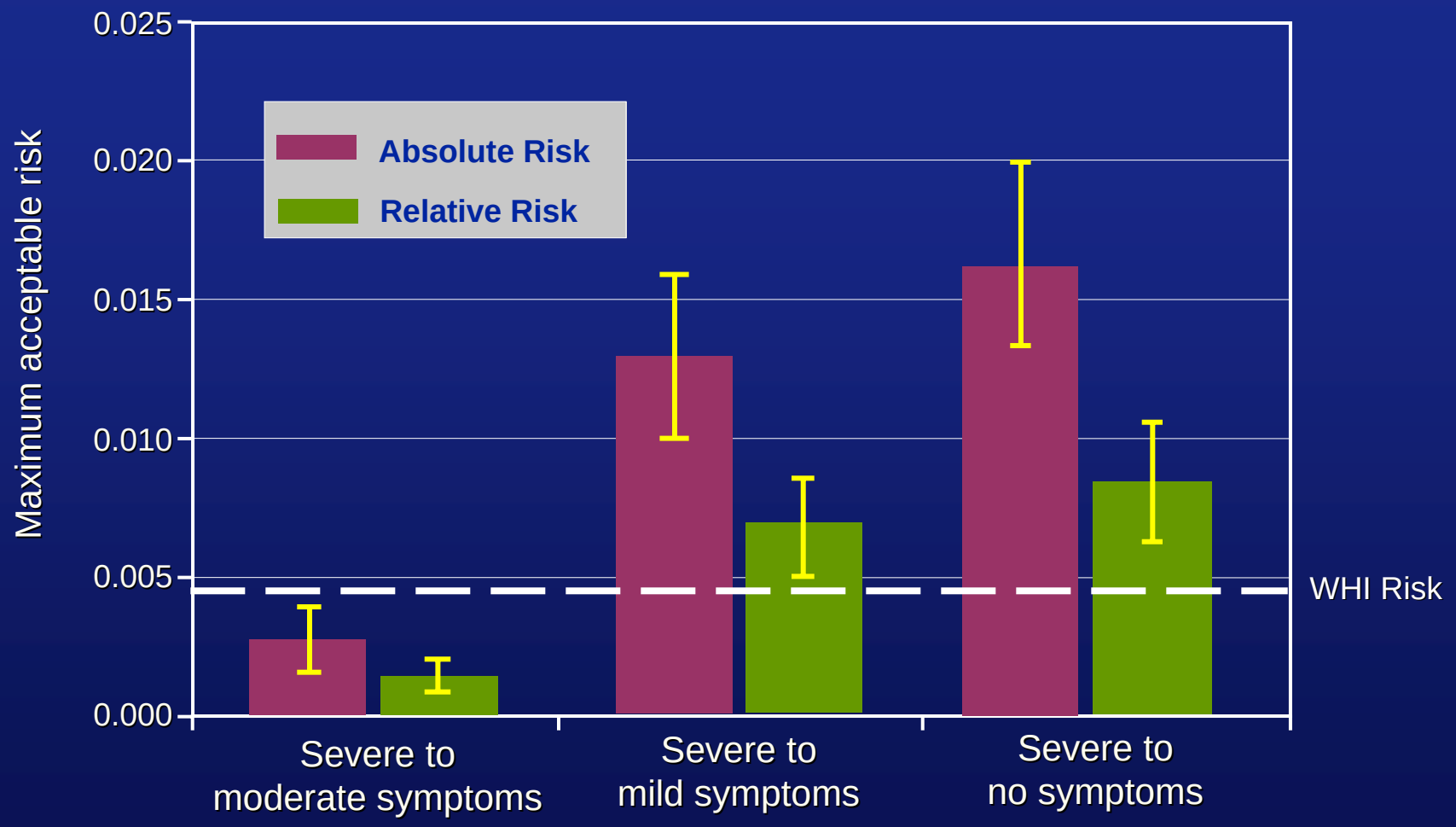
Treatment Feature	Results of Treatment A	Results of Treatment B
Intensity of daytime hot flashes	Mild	Severe
Frequency of daytime hot flashes	1 – 2 times a day	More than 6 times a day
Frequency of night sweats	None	1 – 3 times a night
Duration of hot flashes and night sweats	7 years	1 year
Risk of hip or back fractures within 10 years	↓ 50% decrease in risk	↓ 50% decrease in risk
Risk of heart attack within 10 years	↓ 25% decrease in risk	↑ 30% increase in risk
Risk of breast cancer within 10 years	No change in risk	↓ 25% decrease in risk

Check the box that best describes your opinion

A is much better	A is somewhat better	A and B are the same	B is somewhat better	B is much better
☐	☐	☐	☐	☐

Vasomotor Symptoms

MAR—Breast-Cancer Risk



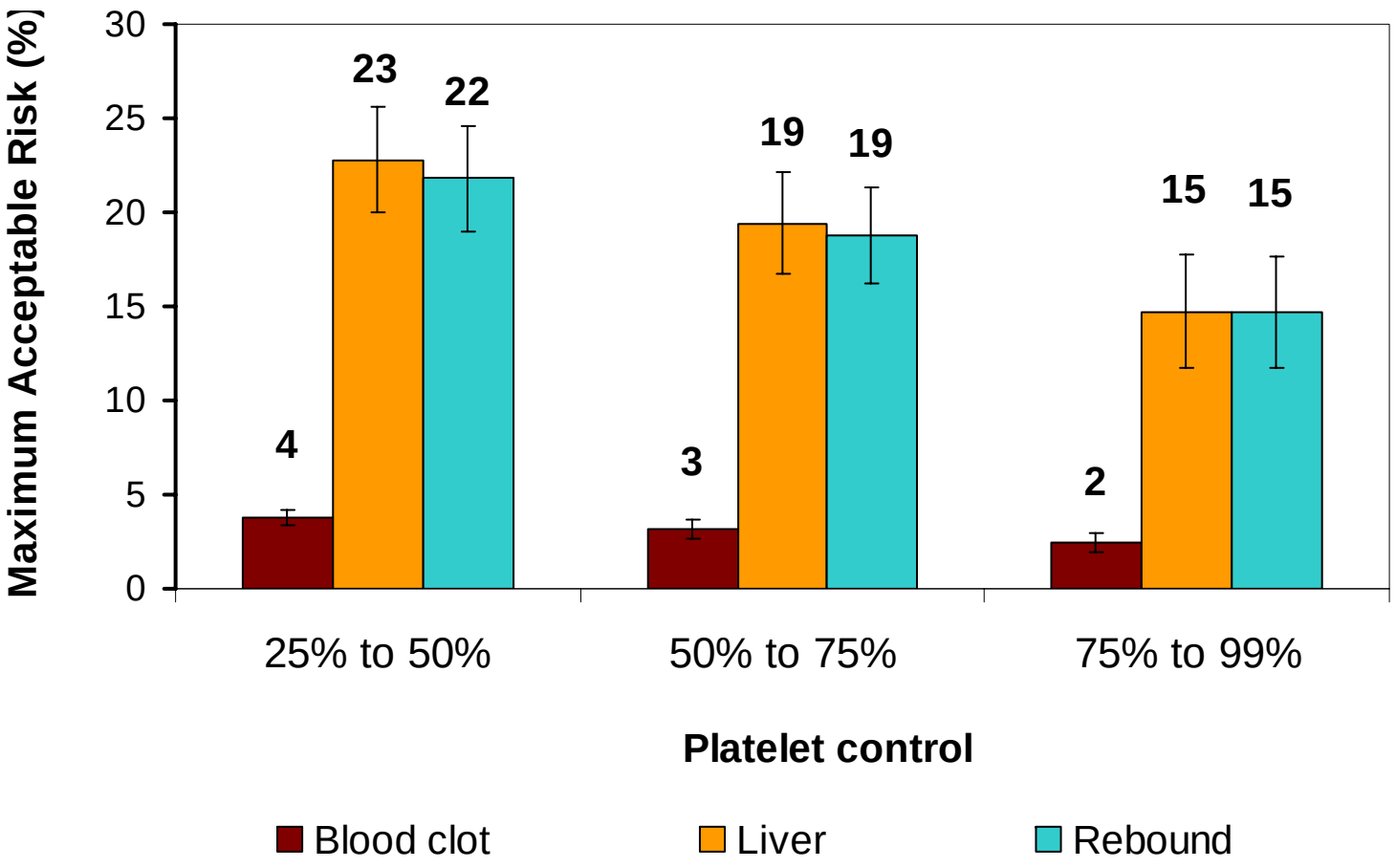
Idiopathic Thrombocytopenic Purpura (ITP)

Maximum Acceptable Risk

Medicine Feature	Medicine A	Medicine B
Chance that the medicine will raise your platelet count to a safe level	75 out of 100 patients (75%)	10 out of 100 patients (10%)
You need to take steroids	Yes	Yes
Chance that the medicine will make your platelet count worse after you stop taking the medicine	10 out of 100 patients (10%)	2 out of 100 patients (2%)
How you take the medicine	1 to 2 pills per day	4 to 8 hour IV infusion once a month at doctor's office
Chance that you have to stop taking the medicine because of liver-function test results	None	None
Chance that the medicine will give you a serious blood clot	5 more out of 100 patients (5%)	2 more out of 100 patients (2%)

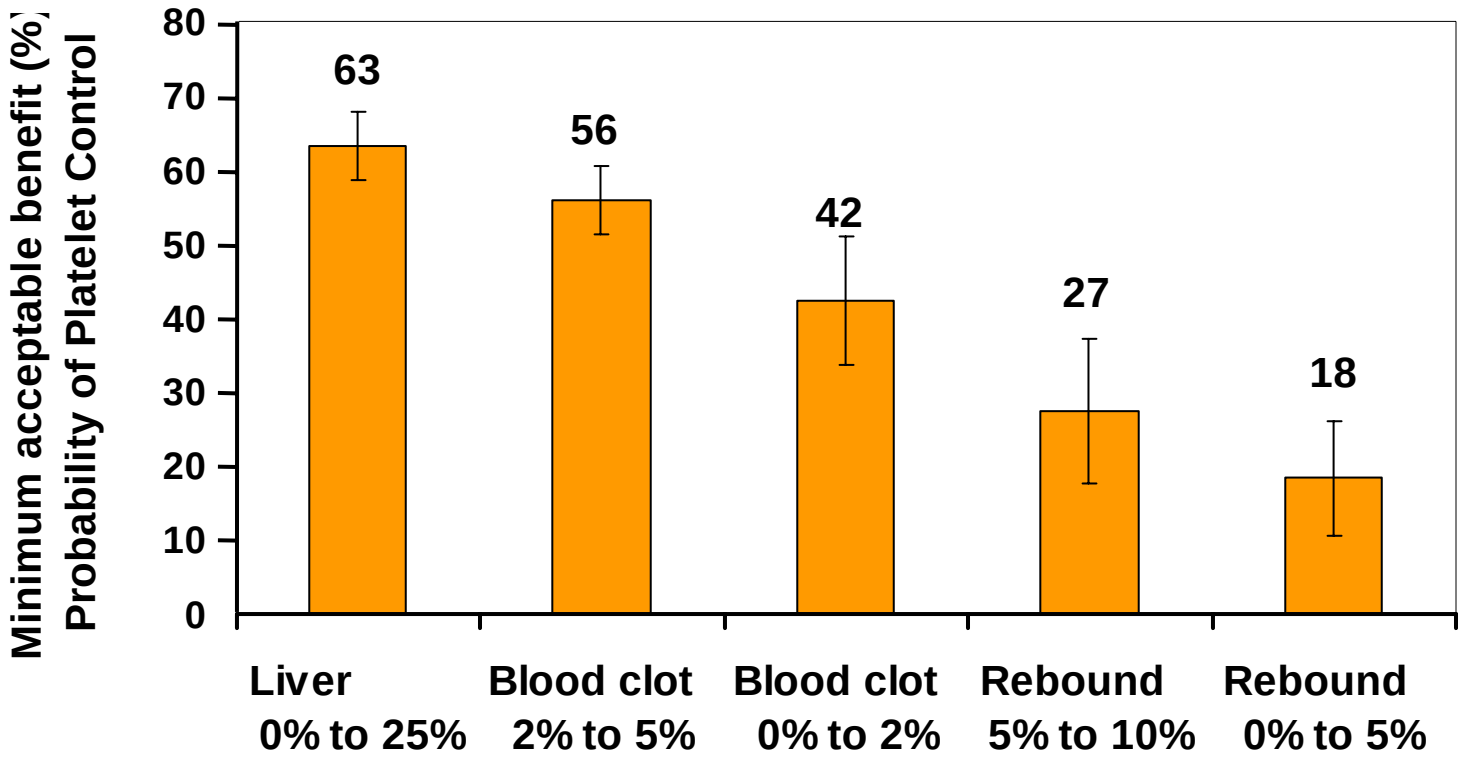
Idiopathic Thrombocytopenic Purpura (ITP)

Maximum Acceptable Risk



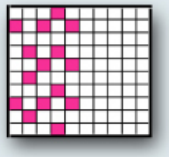
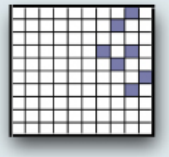
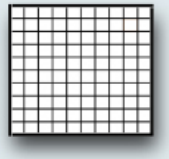
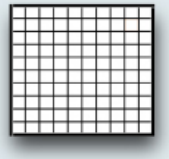
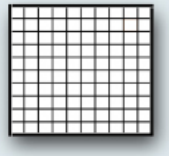
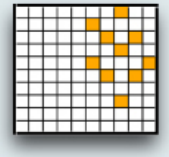
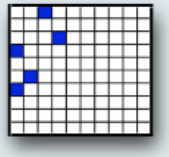
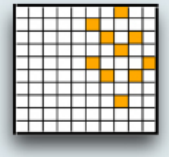
Idiopathic Thrombocytopenic Purpura (ITP)

Minimum Acceptable Benefit



HIV

Choice Task

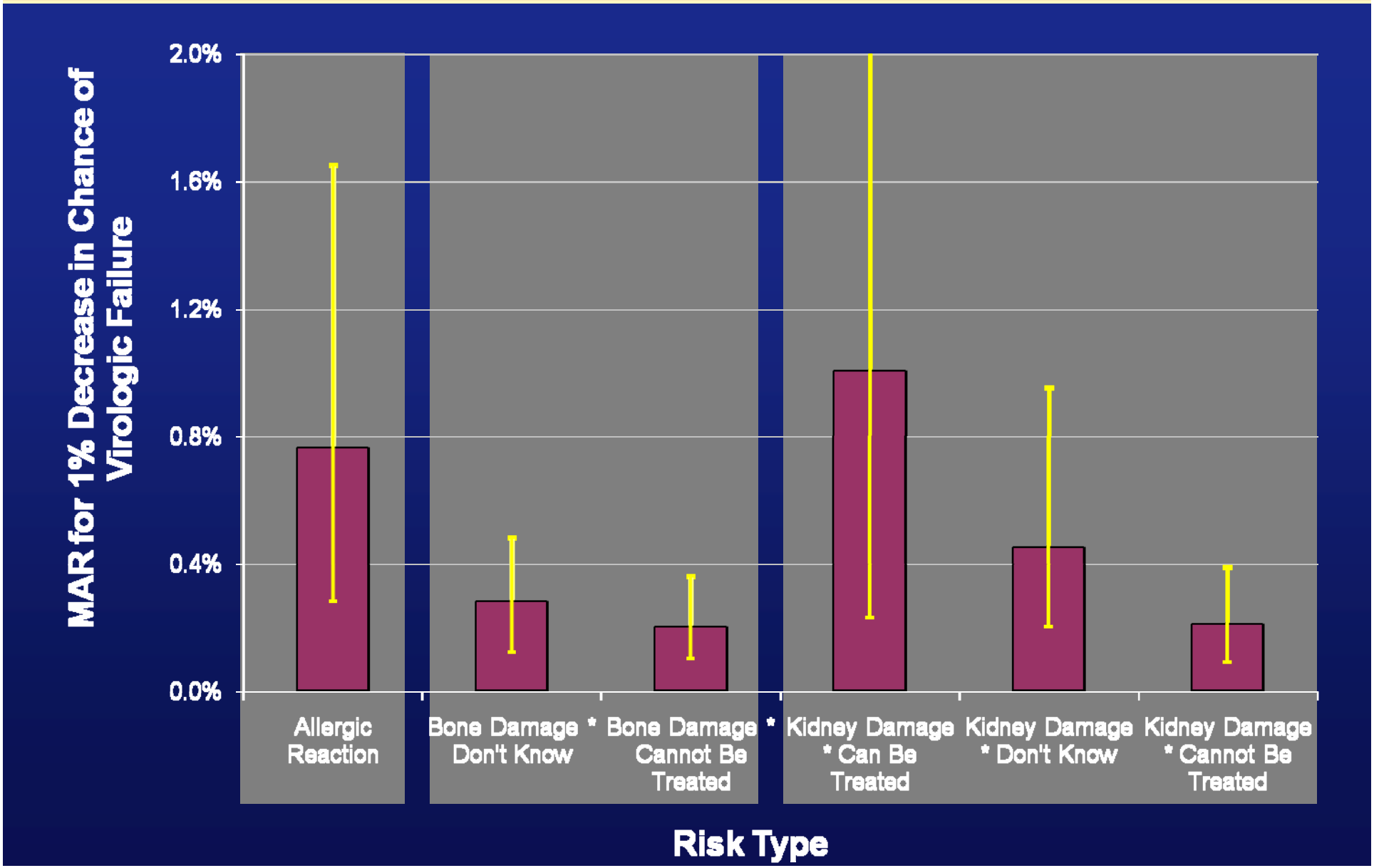
Medicine Feature	Medicine A		Medicine B	
CHANCE THAT MEDICINE DOES NOT WORK		15 people out of 100 (15%)		7 people out of 100 (7%)
CHANCE OF ALLERGIC REACTION		No person out of 100 (0%)		No person out of 100 (0%)
CHANCE OF BONE DAMAGE		No person out of 100 (0%)		10 people out of 100 (10%)
CHANCE OF KIDNEY DAMAGE		5 people out of 100 (5%)		10 people out of 100 (10%)
WHAT HAPPENS IF YOU HAVE BONE OR KIDNEY DAMAGE	Problem cannot be treated successfully		Problem can be treated successfully	

Which medicine would you choose if these were the only options available?

- Medicine A
- Medicine B

HIV

Maximum Acceptable Risk



Discussion

- **Results encouraging, but validity needs more testing**
- **Challenges**
  - Low level of numeracy
  - Complexity of methods
  - Clinician skepticism
- **Next steps**
  - PhRMA case studies
  - More effective communication of results to regulators and physicians
  - Better collaboration among researchers