

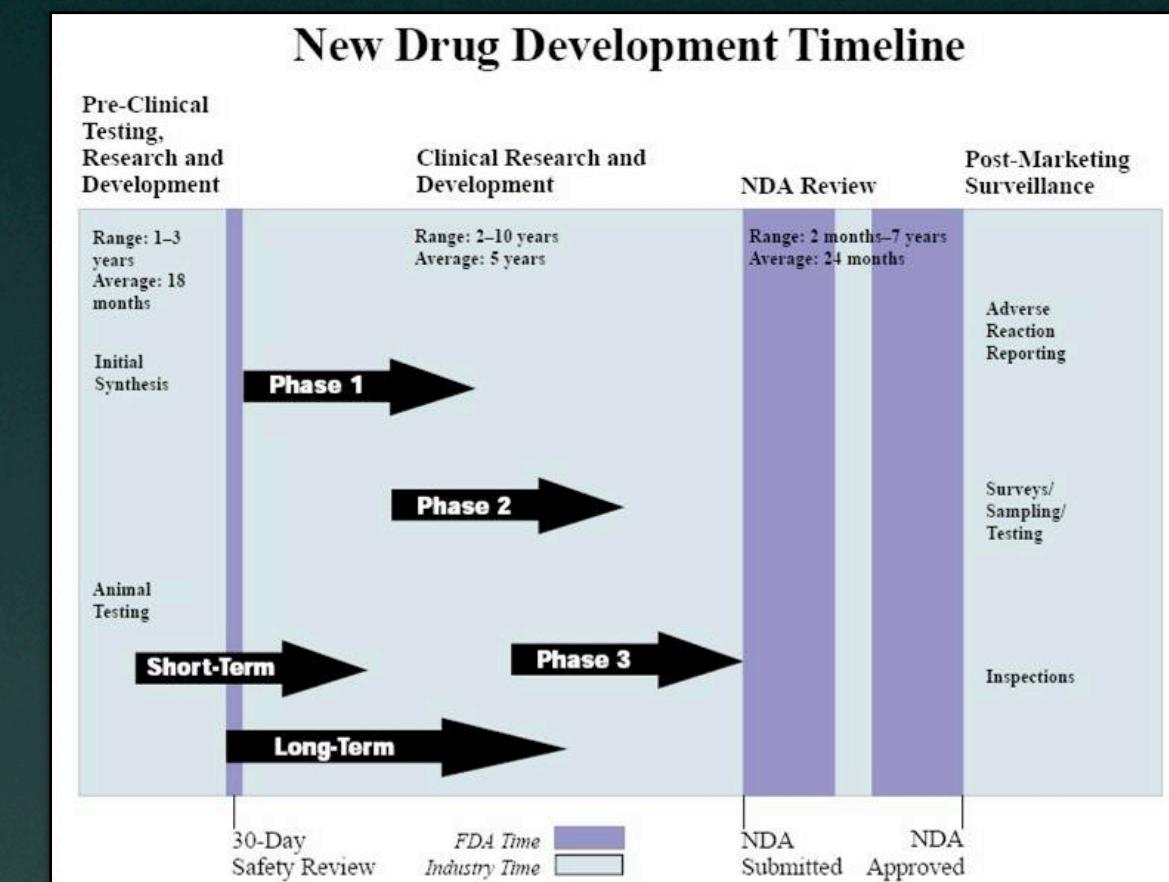
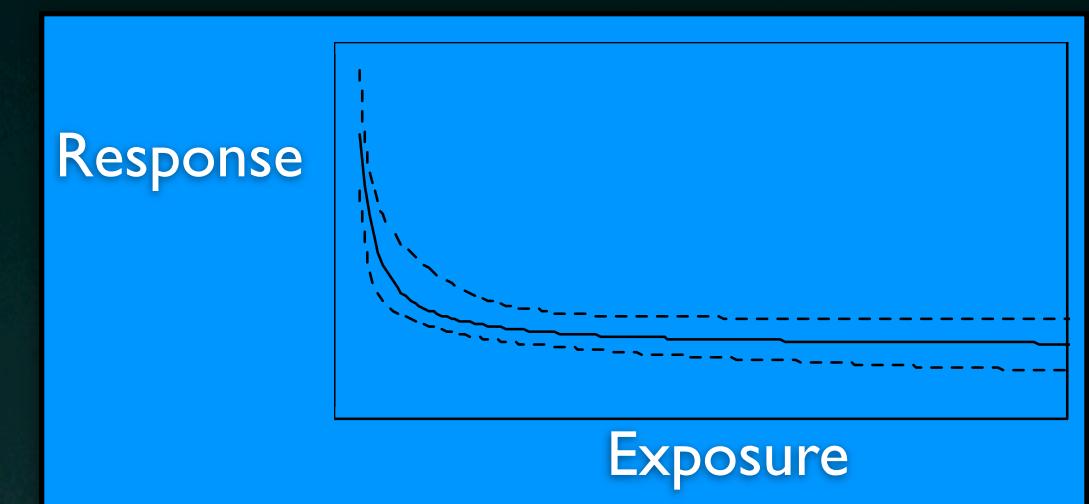
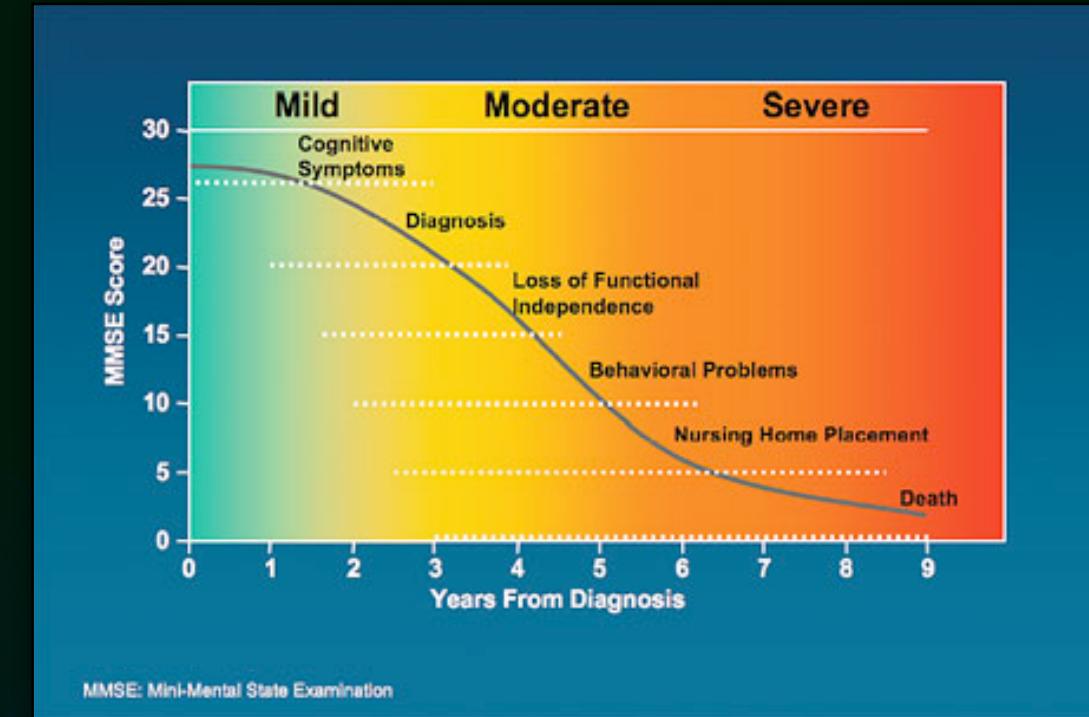
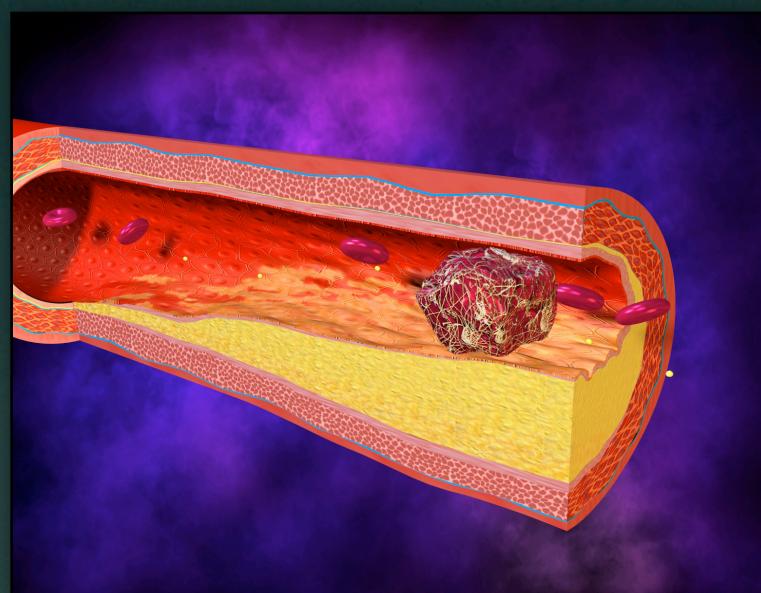
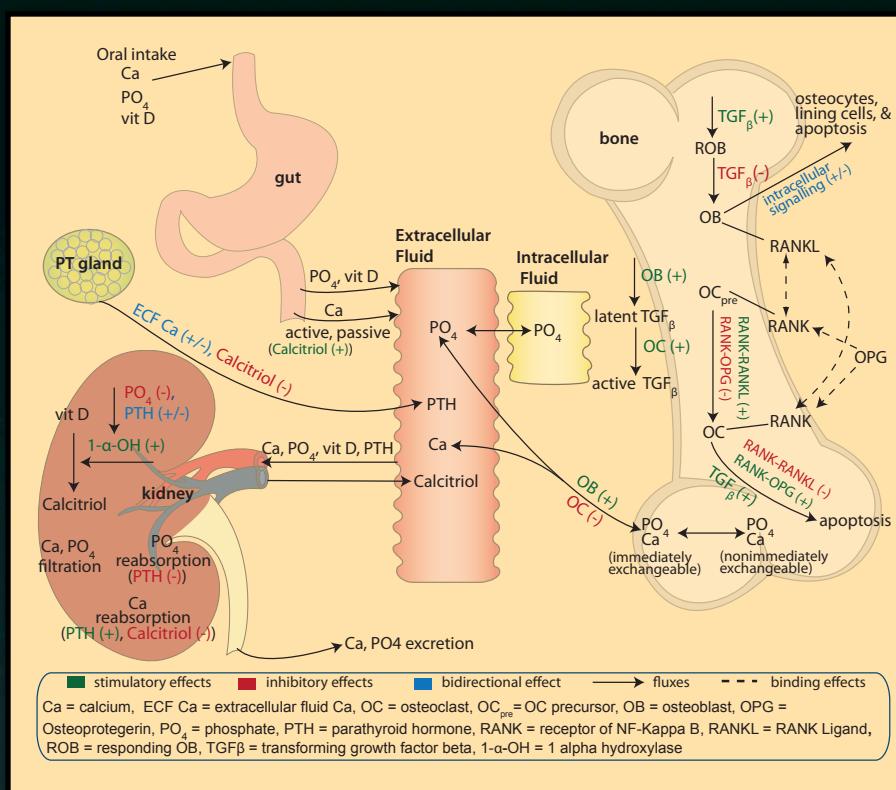
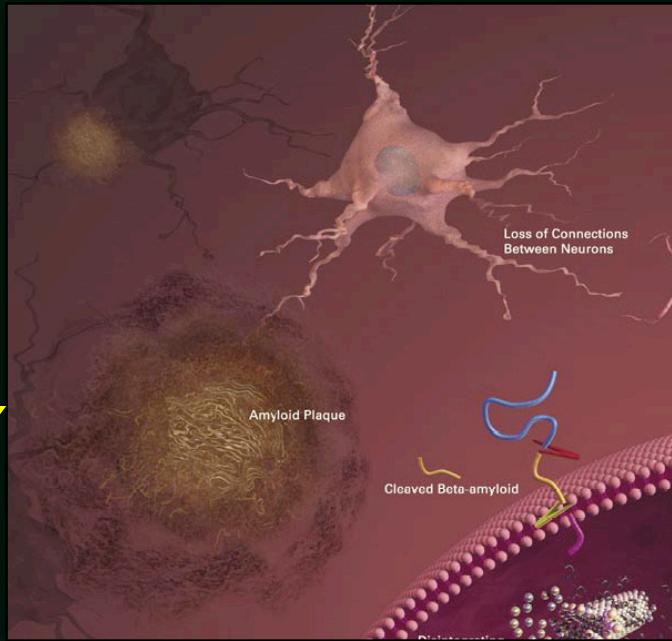
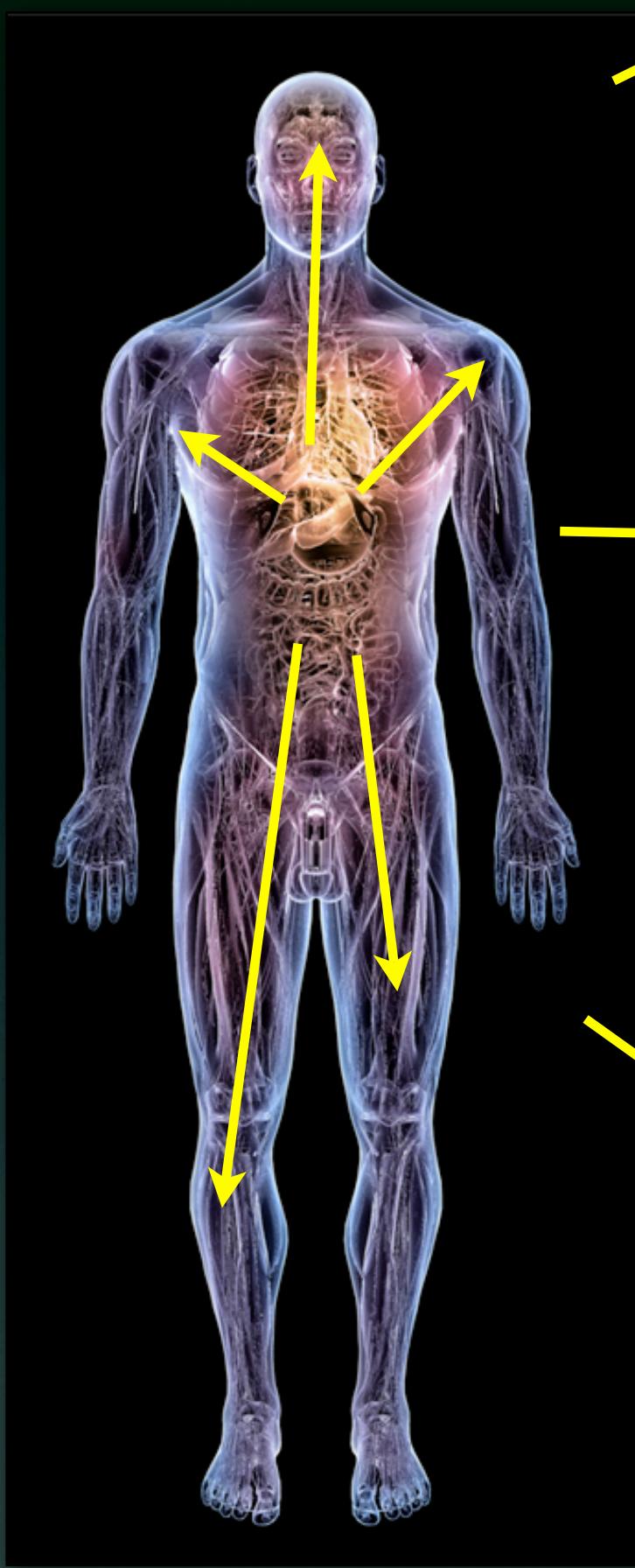
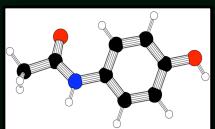
# Modeling and Simulation in Drug Development and Clinical Therapeutics



2008 Capitol Hill M&S Expo



# Building Models and Simulating Outcomes



# Why M&S ?

- Clinical trials are most costly component of drug development
  - \* \$, patients, time
- Historically, too many flawed, failed or useless trials
  - \* Value in early detection of failures
  - \* More informative trials are essential
- Getting the dose right is paramount
  - \* Improve patient outcomes
  - \* Avoid post-marketing changes/withdrawals

*Decreases in Capitalized Cost per Approved New Drug from Shorter Development and Review Times*

Reduction in phase length	REDUCTION IN COST				
	Pre- clinical	Phase I	Phase II	Phase III	Reg. Review
10%	1.0%	0.6%	1.6%	2.3%	1.6%
20%	2.0%	1.1%	3.1%	4.6%	3.1%
30%	2.9%	1.7%	4.6%	6.9%	4.6%
40%	3.8%	2.2%	6.1%	9.0%	6.1%
50%	4.7%	2.7%	7.5%	11.2%	7.6%

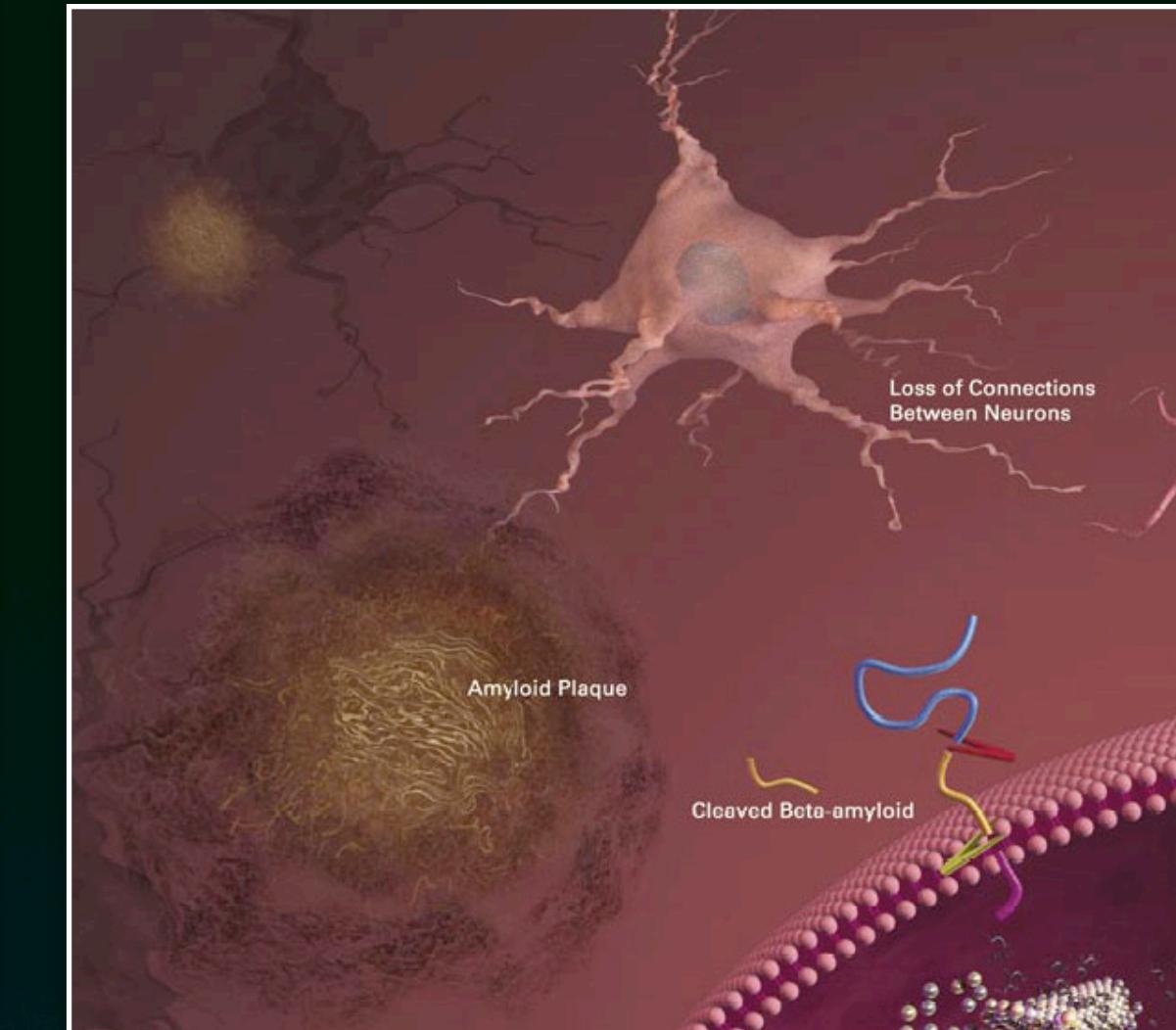
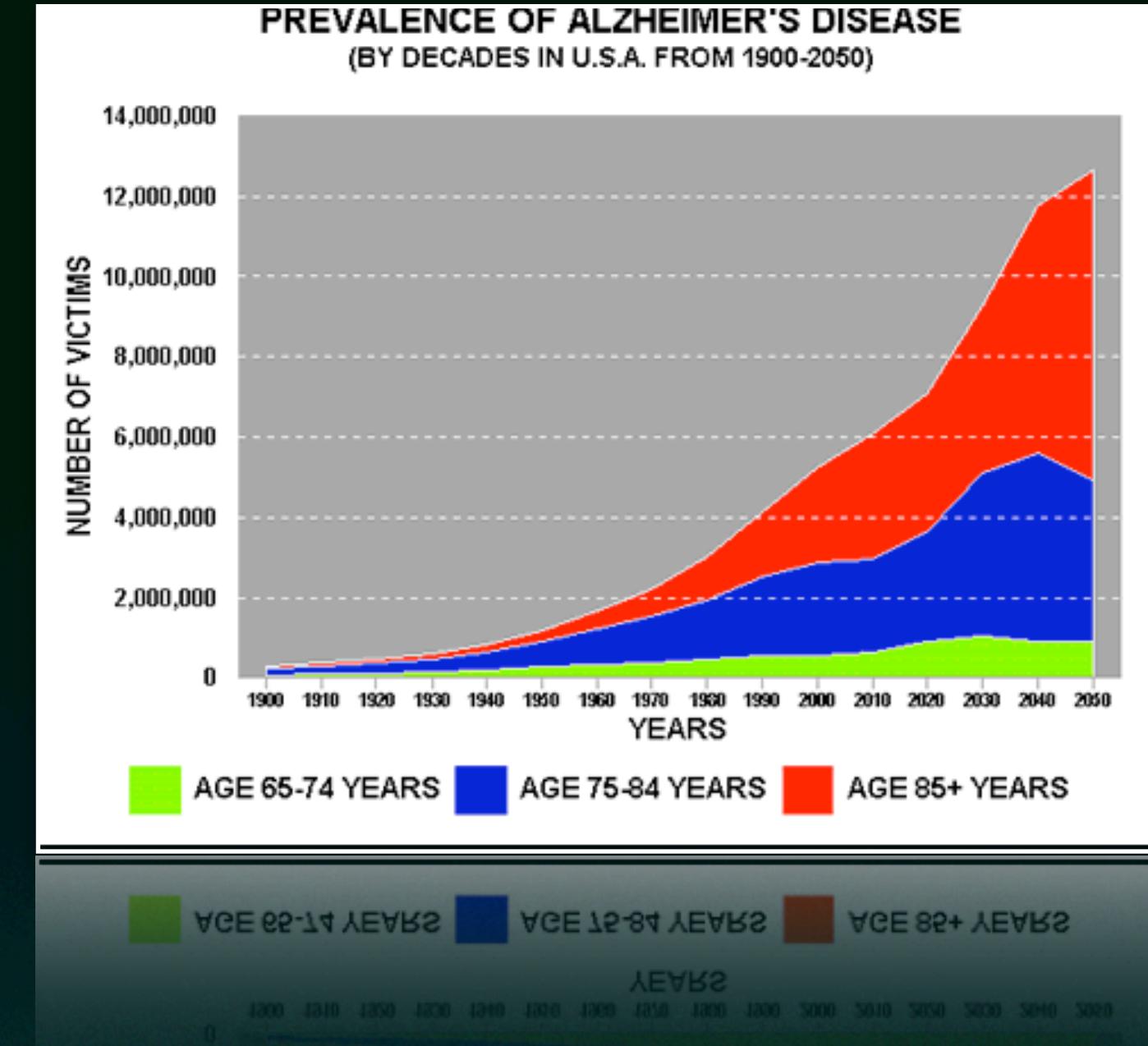
*Source: Tufts Center for the Study of Drug Development*

*Decreases in Out-of-Pocket and Capitalized Clinical Cost per Approved New Drug from Shifting Failures from Phase II to Phase I*

% of investi- gational drugs shifted to earlier failure	REDUCTION IN CLINICAL COST			
	Out-of- pocket	Capital- ized	Out-of- pocket (Adjusted for different costs for failures)	Capital- ized
5%	1.5%	1.6%	0.9%	0.9%
10%	3.0%	3.2%	1.8%	1.9%
15%	4.6%	4.9%	2.6%	2.8%
20%	6.1%	6.5%	3.5%	3.8%
25%	7.6%	8.1%	4.4%	4.7%

*Source: Tufts Center for the Study of Drug Development*

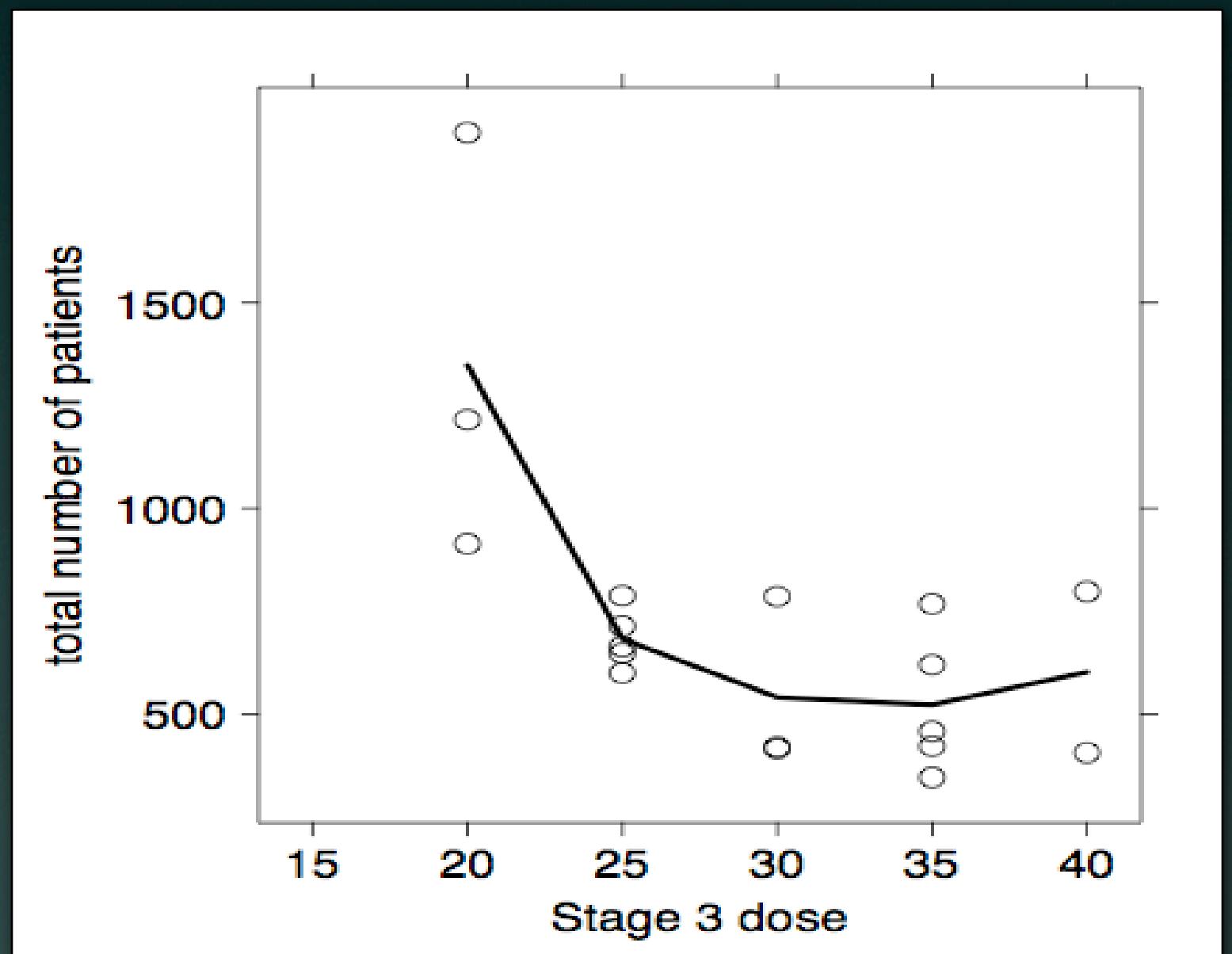
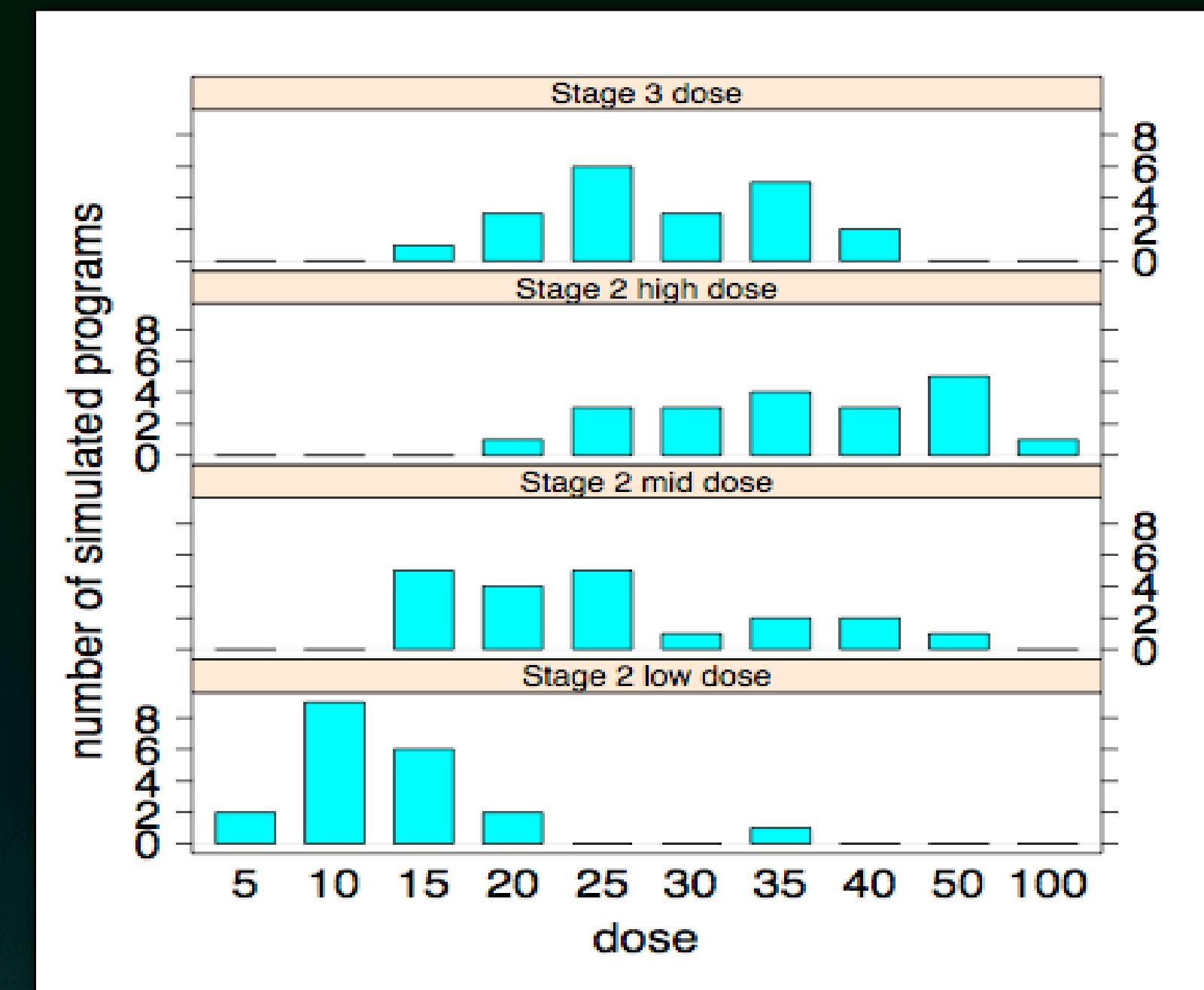
# Alzheimer's Disease



- Growing patient population
- Central nervous system disease mechanism
- Long-term trials
- Active R&D but lack of disease modifying therapies

# M&S - Optimized Trial Design & Implementation

- Model-based adaptive trial design
- Decision rules based on:
  - \* Efficient and accurate dose selection
  - \* Accuracy of efficacy determination
  - \* Minimized development duration



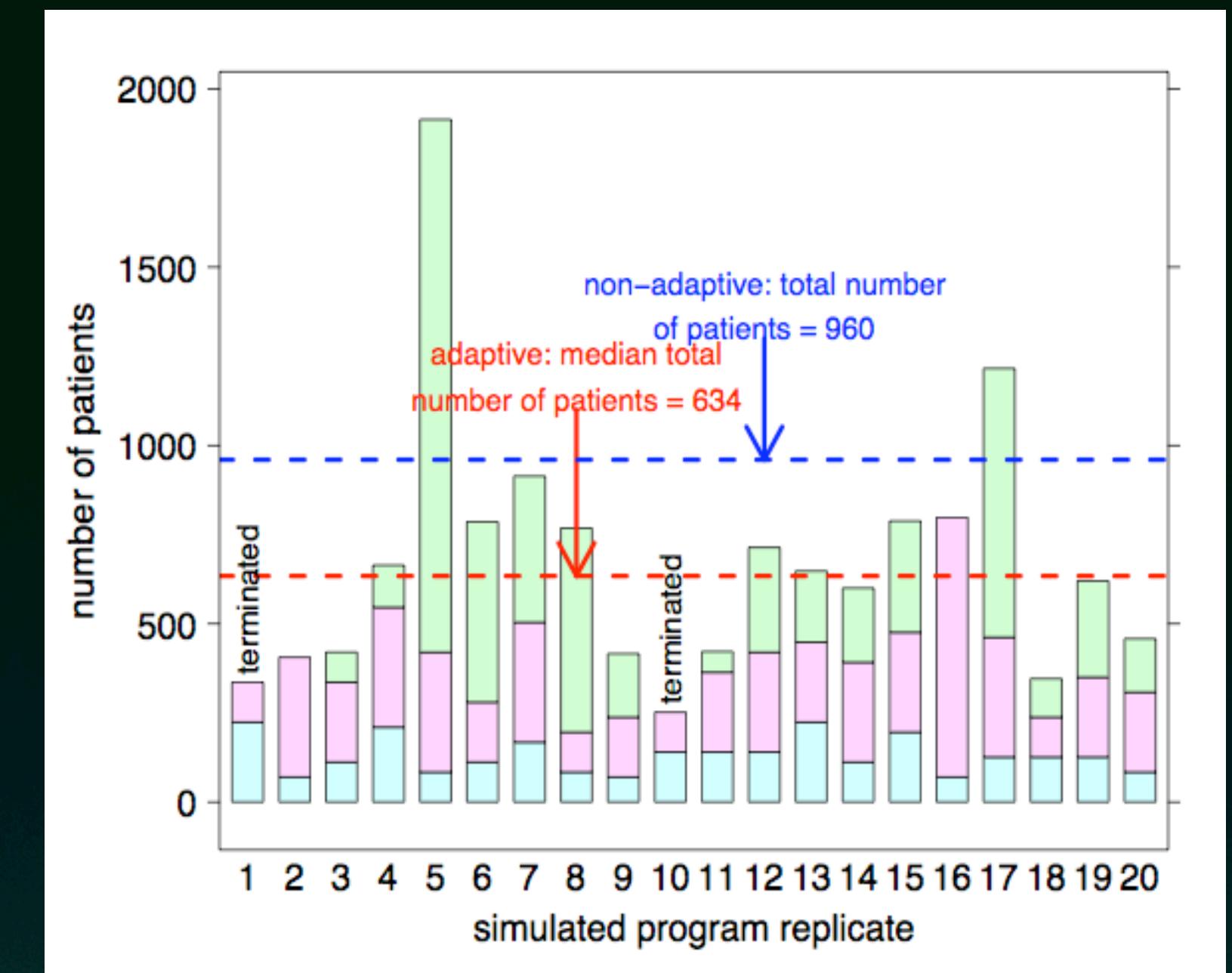
# AD Simulated Trial Results

Model-based adaptive trial performance compared to traditional approaches:

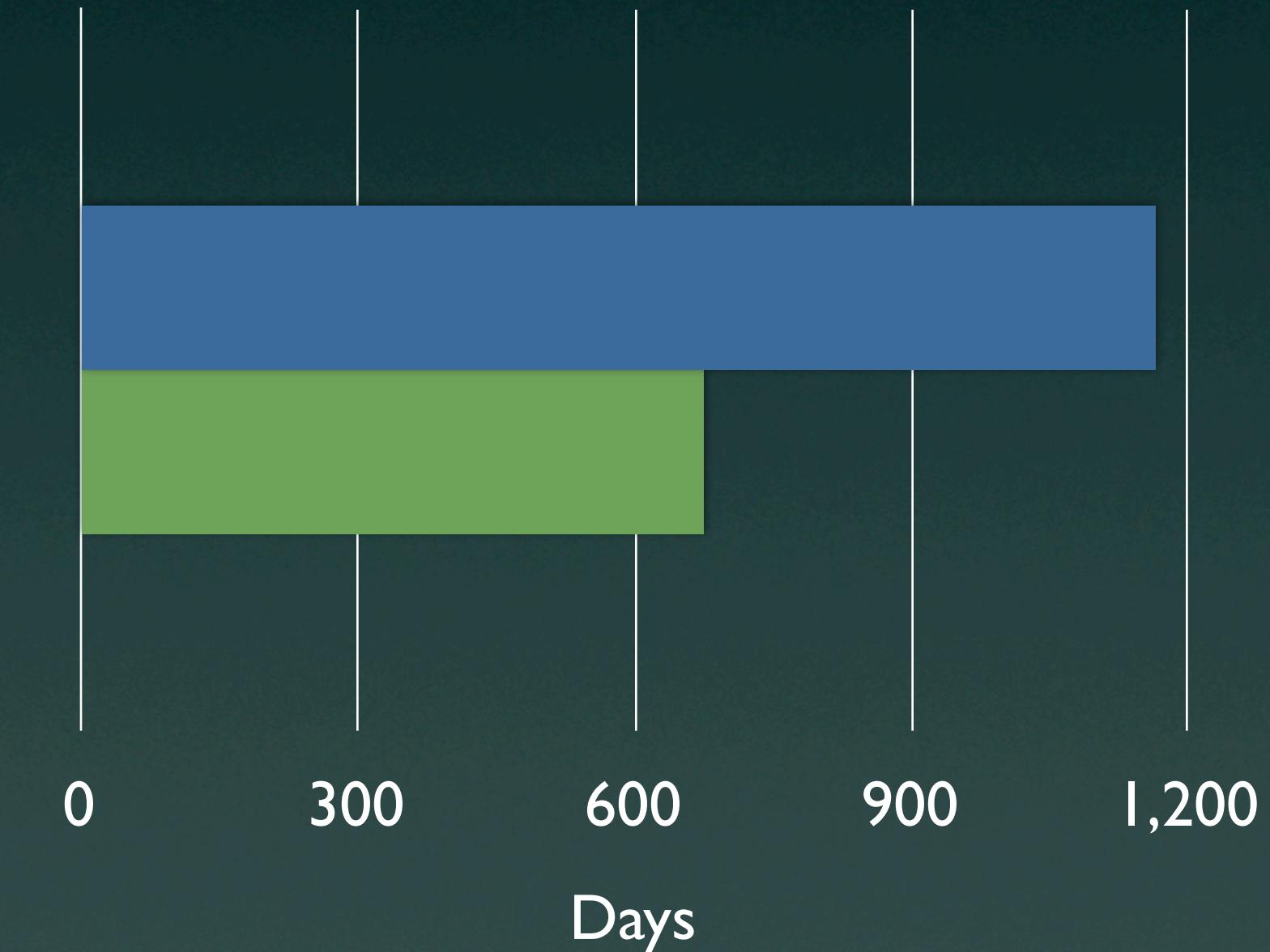
- Accurate dose selection
- Efficient determination of efficacy or futility
- Decreased overall development time

\* almost 1 year gain on patent life

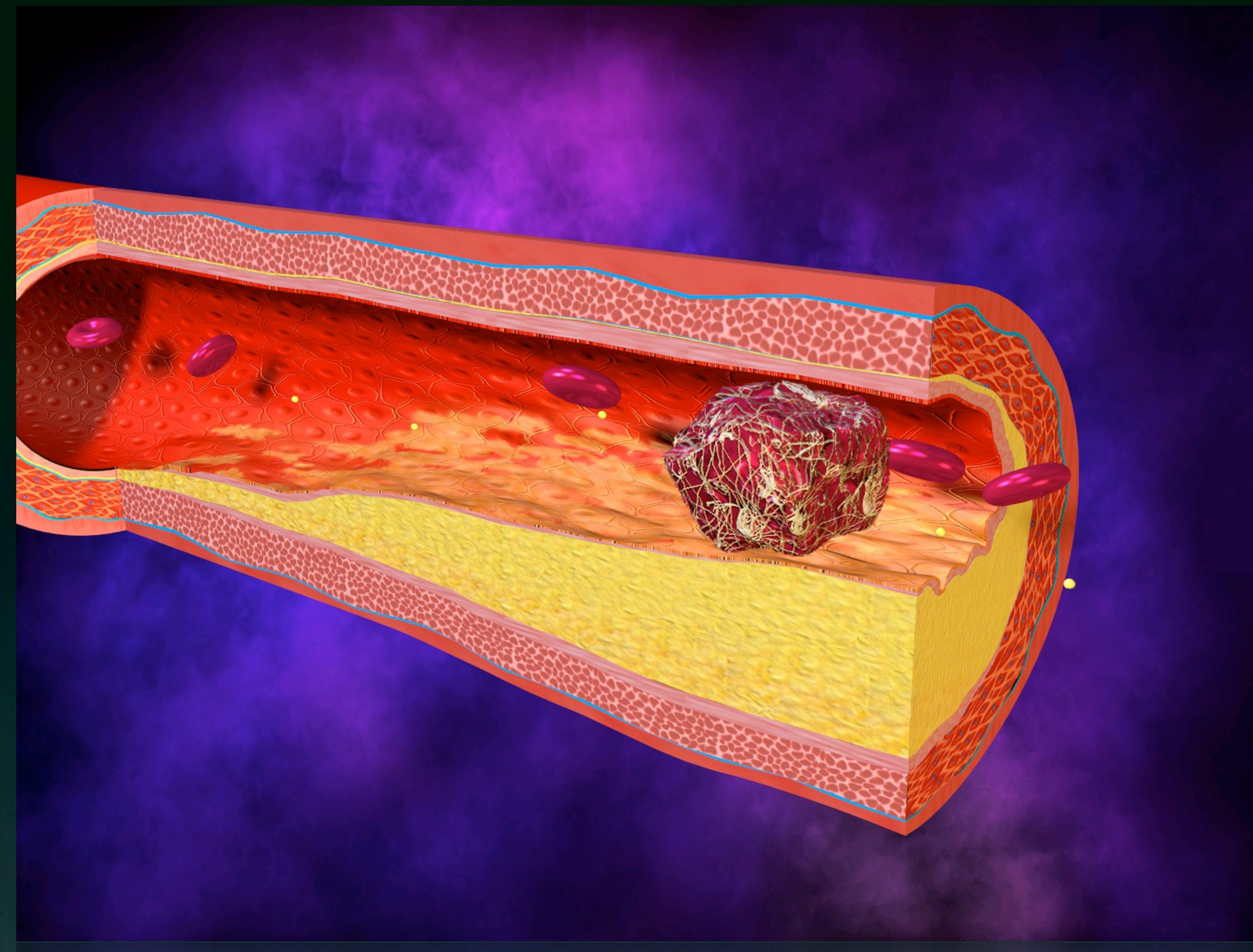
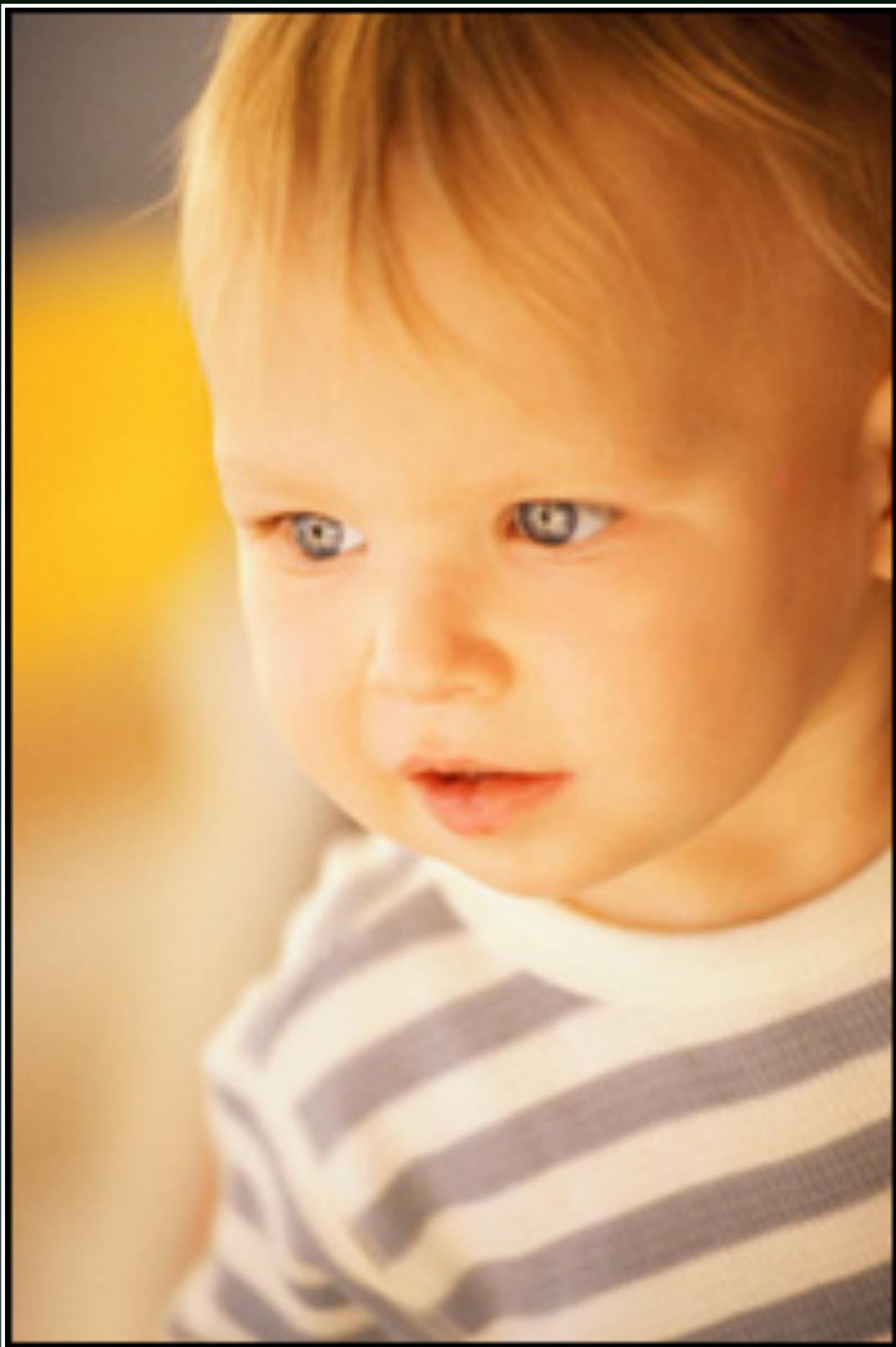
\* ~ 330 fewer patients



Traditional      Model-Based



# Pediatrics



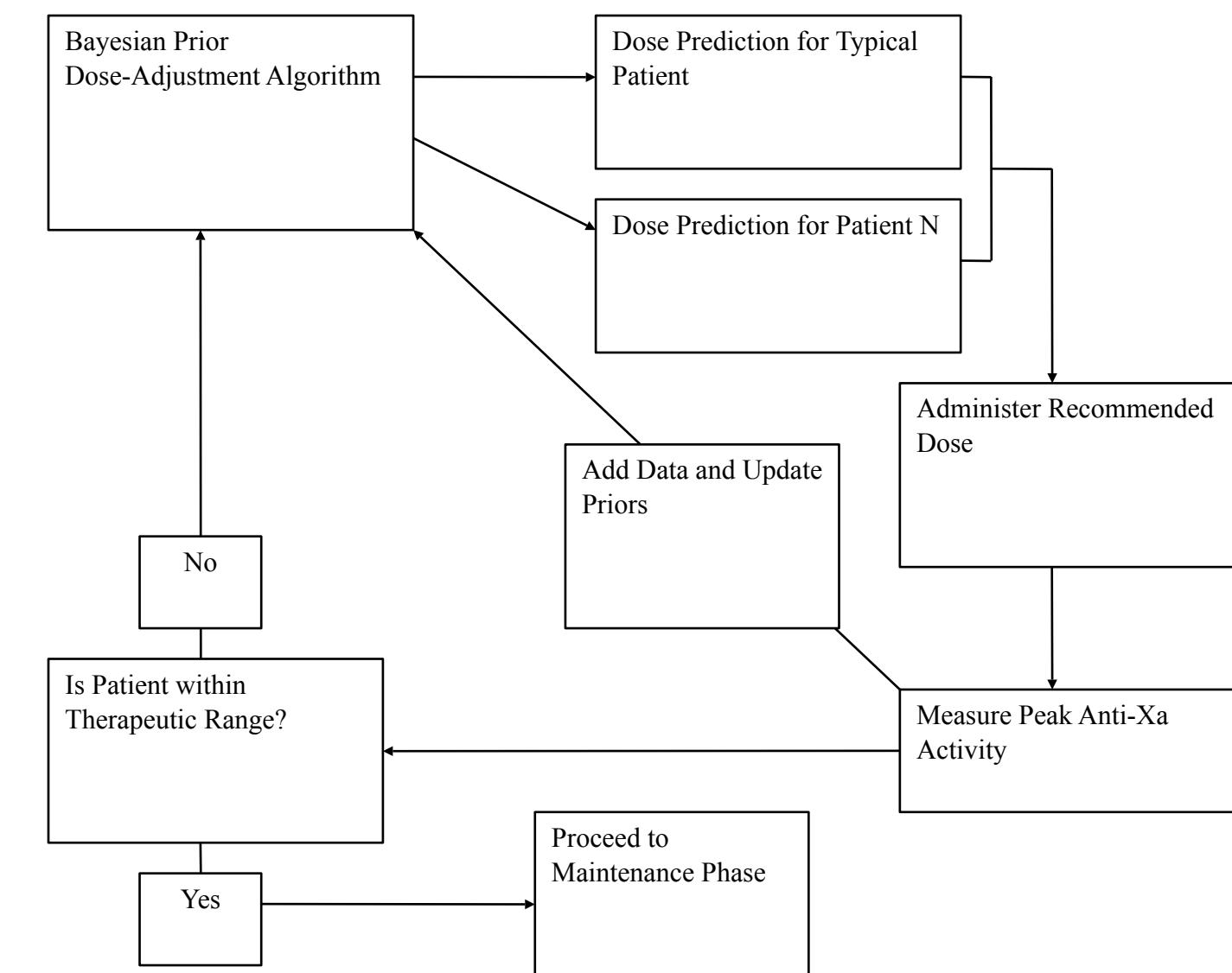
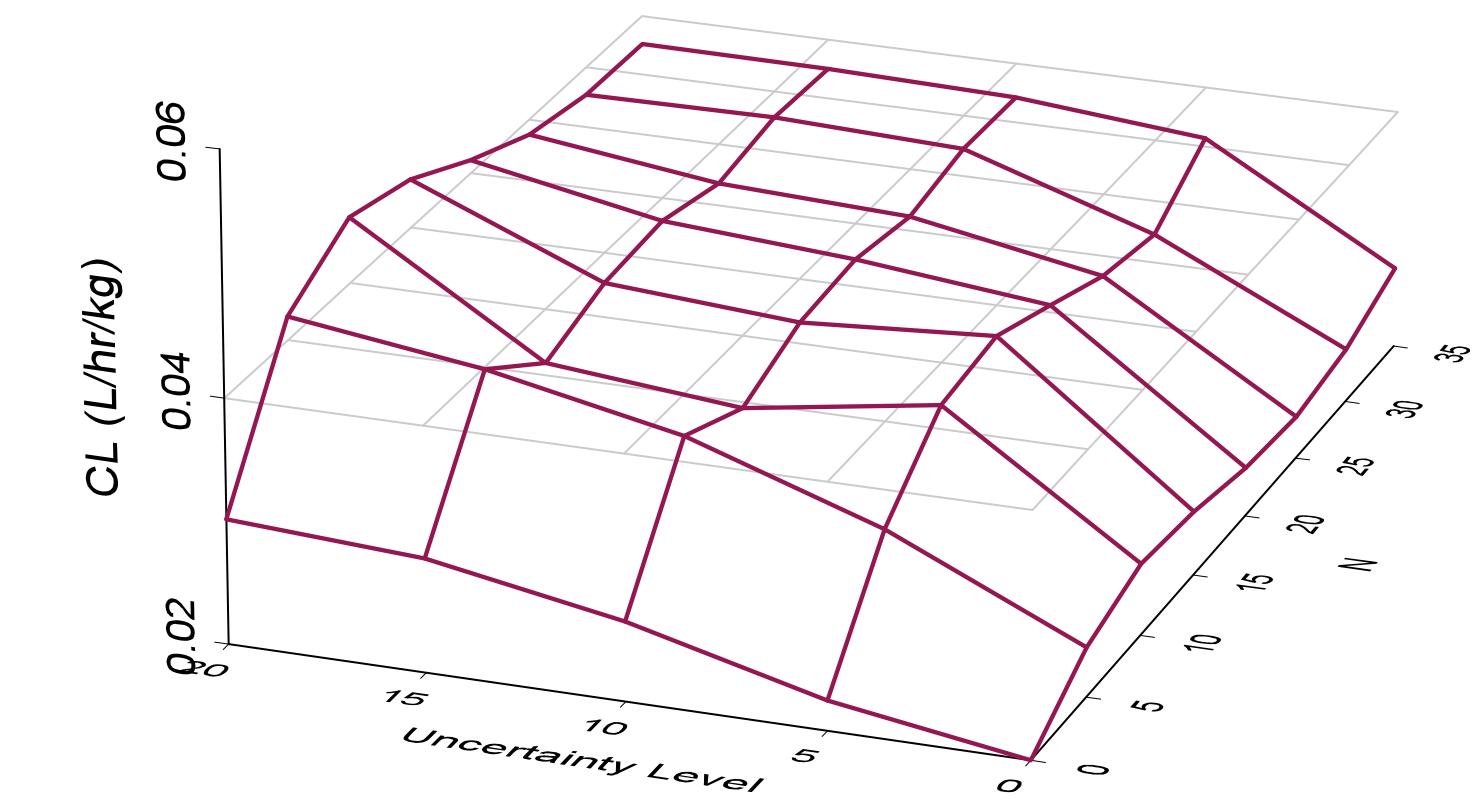
- New anti-coagulant drug (LMWH)
- First trials in pediatrics
- Efficient individualization of dosing is critical

# M&S - Optimized Trial Design and Dosing

Pediatric trial performance explored by M&S

Goal: Develop individual dosing algorithm

- \* Maximize efficacy
- \* Minimize toxicity



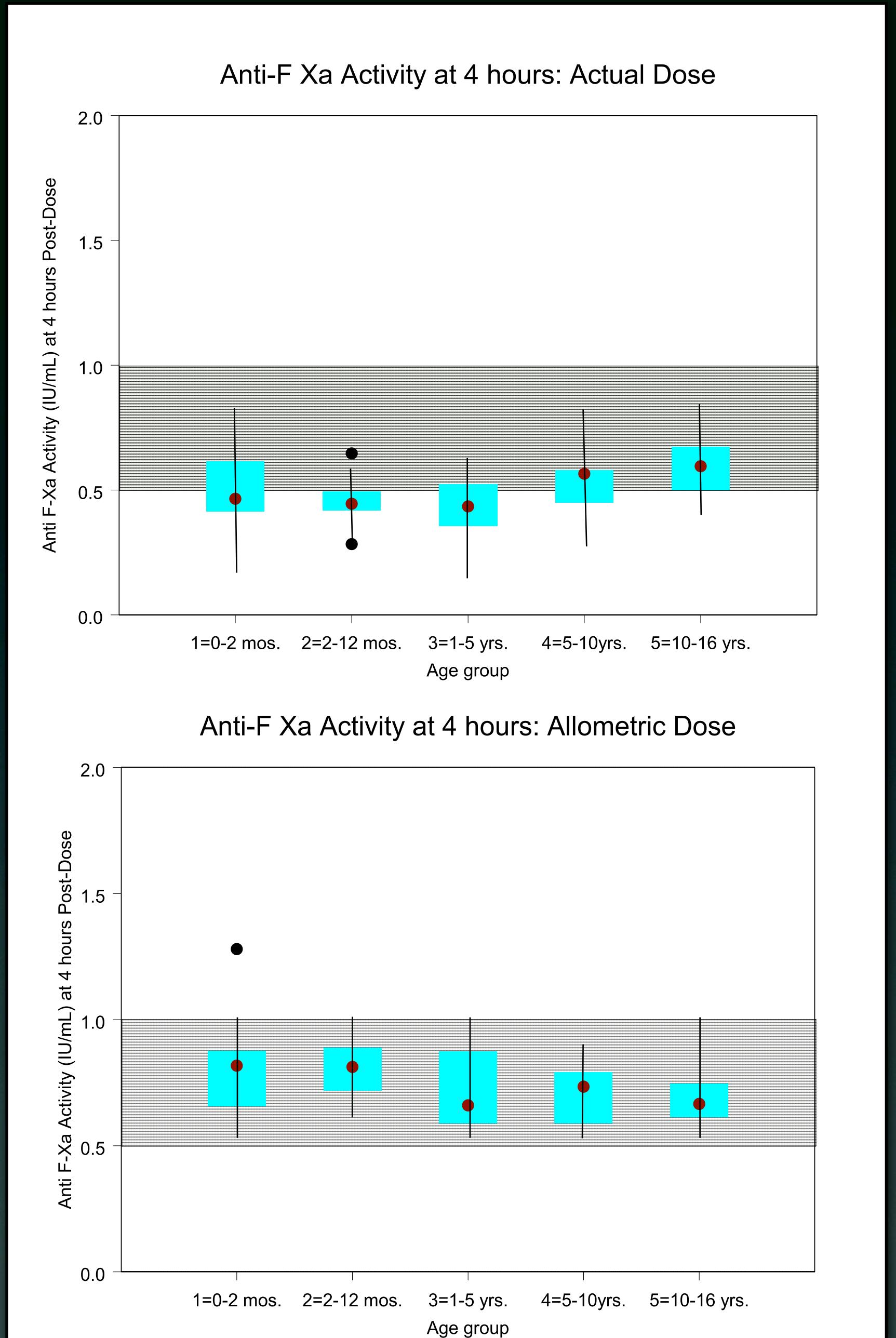
# Pediatric Trial M&S Results

Actual trial executed using traditional dosing guidance:

- Unacceptable lack of efficacy in younger patients

New dosing guidance:

- Based on M&S
- Improved efficacy and safety across the age range



# M&S in Drug Development and Clinical Therapeutics

- Build knowledge
- Support decision making
- Increased efficiency and informativeness:
  - \* Pharma/Biotech Development
  - \* Government-Sponsored Clinical Trials
- Better drugs, doses & outcomes for patients

