From talking to action.
A personal view on making an impact.

Phil Woodward

Global Head of PTx Statistics

Pfizer

Summary

- What did we do?
- How did it begin?
- What were the obstacles to success?
- Final thoughts and discussion.

What did we do?

- Situation at end of 2008
  - Predominantly frequentist approach to Phase 2
  - Bayesian methods were the exception
- Situation at end of 2010
  - Predominantly Bayesian approach to Phase 2
  - Utilised power of Bayes unless good reason not to
  - Still more to do, but a clear shift in emphasis
- Pros & cons of Bayes is not purpose of this talk
  - Share my views on how change came about

How did it begin?

- A vision of how things could be better.
  - Uncomfortable feeling about the current state
  - Strong desire to have a positive impact
  - Relevant knowledge and experience
  - Position that facilitates broad influence
  - Strong team of statisticians
  - Colleagues open to new ideas

How did it begin?

- Be clear on expectations of Statisticians.
  - Encourage an environment open to new ideas
  - Involvement of all in the change process
  - We will be advocates and leaders of change
- Note: initially not a specific Bayesian focus

My expectations of the statisticians

Joint ownership

COMMITMENT

Show you mean it

Influence,
seek agreement,
and then deliver.

We are scientists too!

THINK

Test your understanding
- invite challenges

Be logical

Pride in your profession

EXCELLENCE

Know your stuff
- sampling theory
- probability theory
- modes of inference

Read, read,
& re-read

Challenge the status quo

BRAVERY

Avoid dogma

Communicating ideas/results
- focus on the “so what?”
- excellent graphics
- software skills

My expectations of the statisticians

Wider "Quant" community

Project Team

Statistics

BE PART OF THE WHOLE

Clinical Research

Your RU, WRD & Pfizer

Go home and relax.

STAY CALM

Don't forget what really matters.

Pressure is good.
Stress is bad.

We're at work for a large percentage of our life!

MAKE IT FUN

Don't wait until you're in a rut.

Know what adds value

FOCUS ON WHAT'S IMPORTANT

Understand the Business imperatives

Obstacles to Success: Bayesian specific

Education & training in Bayesian approach

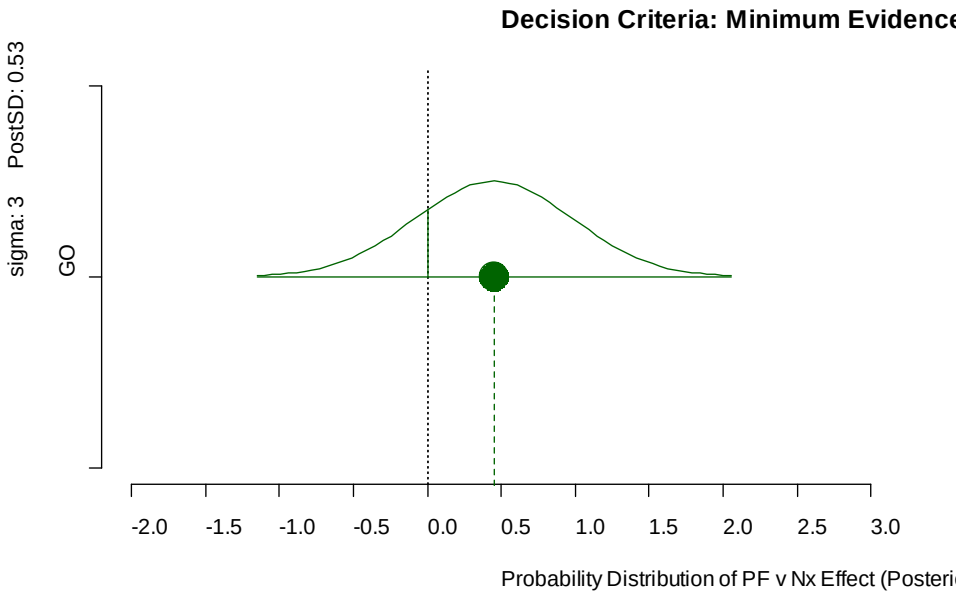
- Philosophy as well as methods
- Determining Priors
  - Historical data: access and exchangeability
  - Elicitation: purpose & “how to do it”
- Software tools for non-experts
  - e.g. BugsXLA GUI for WinBUGS, R Scripts

Precedented methods not available

- What do we do with all the new probabilities?
  - Classical : p(Pass test | true value) : power
  - Bayesian: p(Pass test) : E(power)
    - p(true value | Pass test) : +ve pred. post.
    - p(true value) : prior

Bayesian Decision Criteria

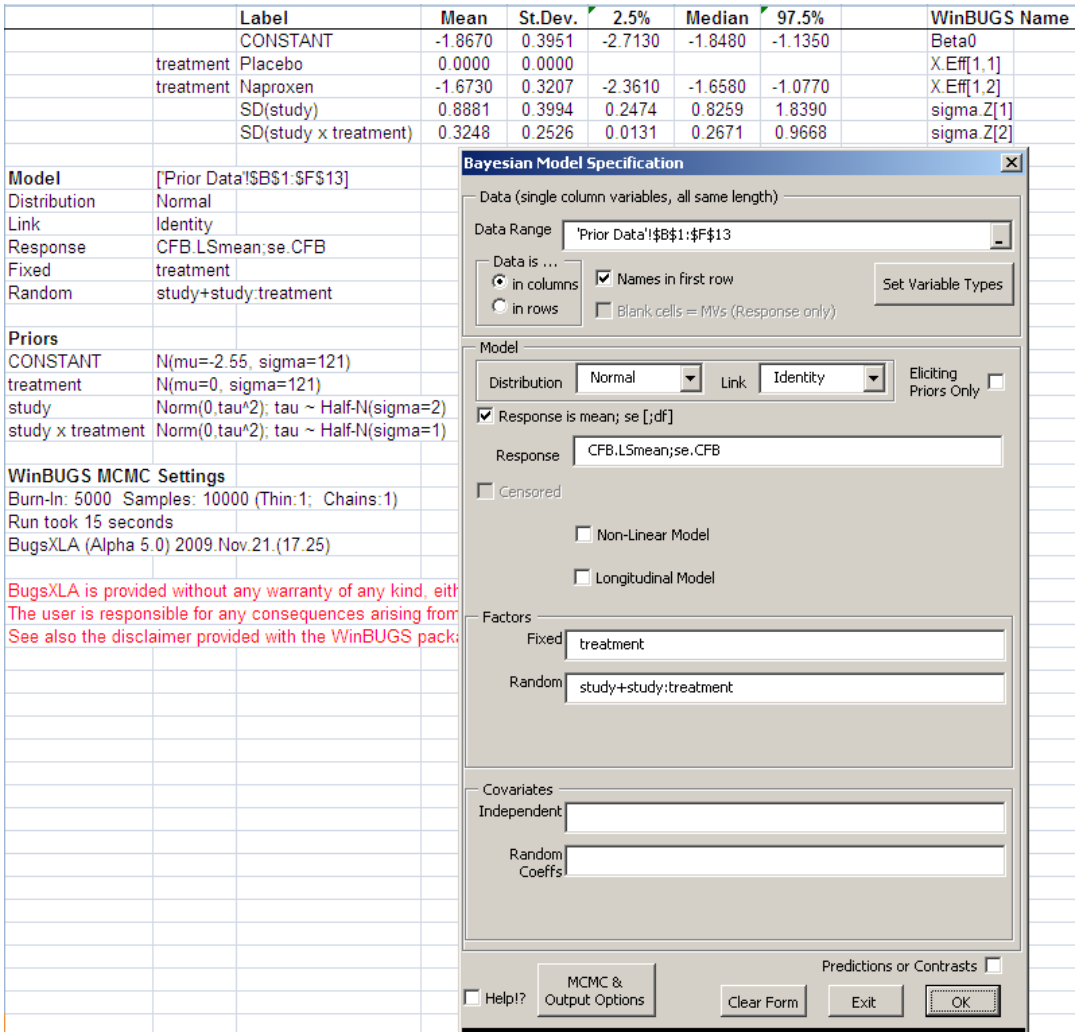
At least 80% sure better than standard of care.



Prior Distributions from Historical Data

Model fitted using WinBUGS via GUI BugsXLA

BugsXLA removes need for WinBUGS expertise

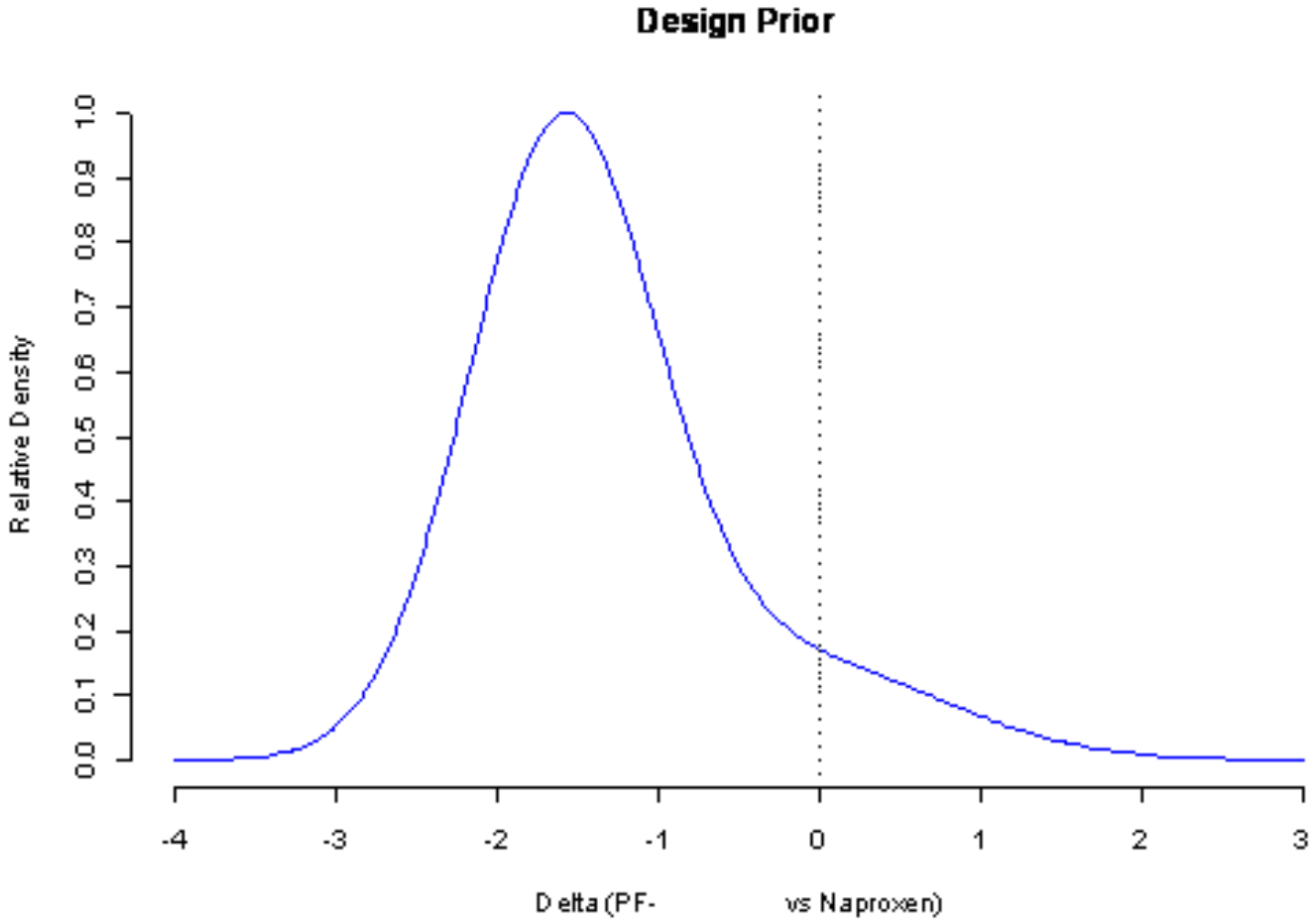


		Label	Mean	St.Dev.	2.5%	Median	97.5%	WinBUGS Name
		CONSTANT	-1.8670	0.3951	-2.7130	-1.8480	-1.1350	Beta0
	treatment	Placebo	0.0000	0.0000				X.Eff[1,1]
	treatment	Naproxen	-1.6730	0.3207	-2.3610	-1.6580	-1.0770	X.Eff[1,2]
		SD(study)	0.8881	0.3994	0.2474	0.8259	1.8390	sigma.Z[1]
		SD(study x treatment)	0.3248	0.2526	0.0131	0.2671	0.9668	sigma.Z[2]

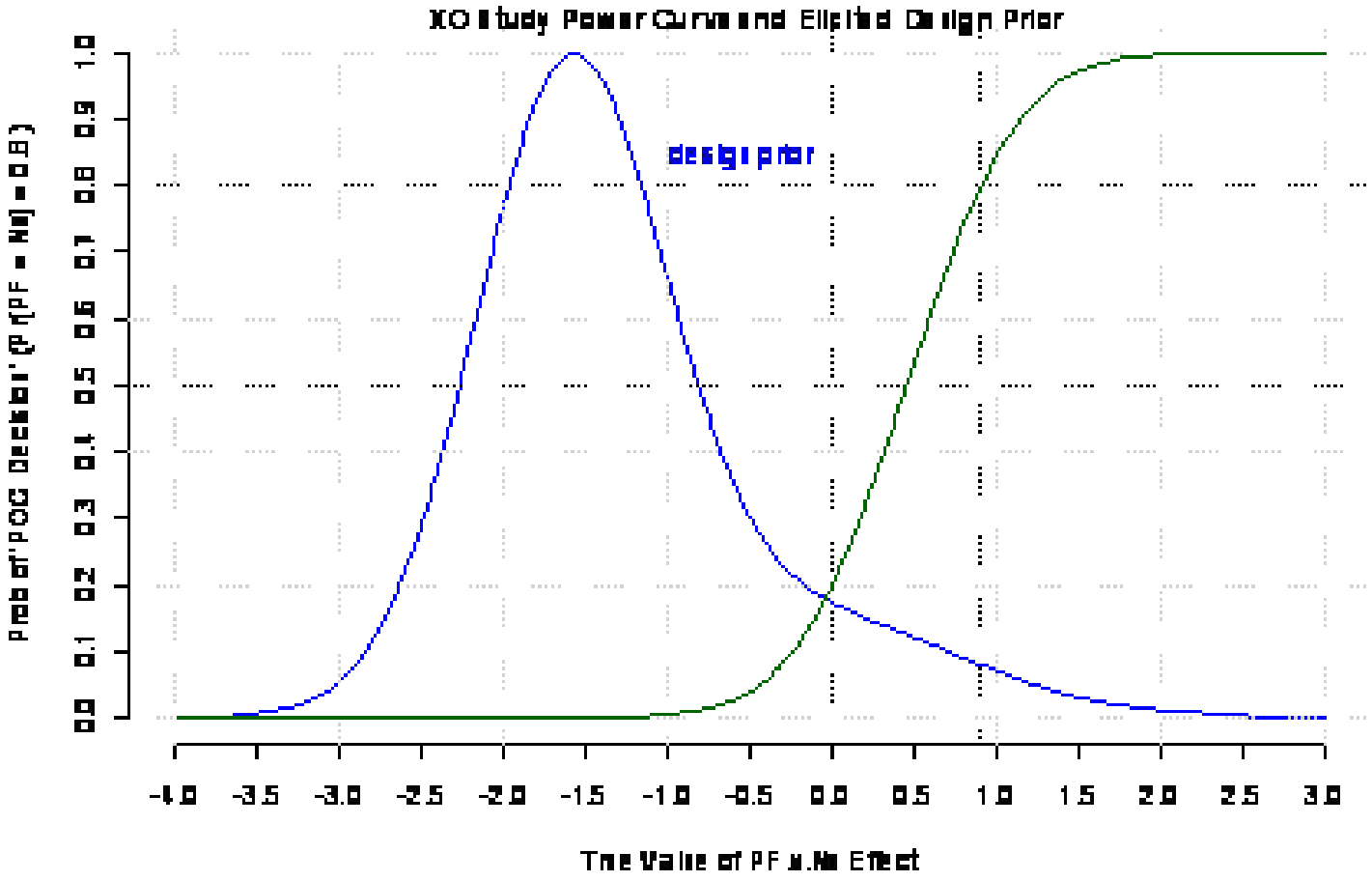
Model	['Prior Data'!$B$1:$F$13]
Distribution	Normal
Link	Identity
Response	CFB.LSmean;se.CFB
Fixed	treatment
Random	study+study:treatment
Priors	
CONSTANT	N(mu=-2.55, sigma=121)
treatment	N(mu=0, sigma=121)
study	Norm(0,tau^2); tau ~ Half-N(sigma=2)
study x treatment	Norm(0,tau^2); tau ~ Half-N(sigma=1)
WinBUGS MCMC Settings	
Burn-In: 5000 Samples: 10000 (Thin:1; Chains:1)	
Run took 15 seconds	
BugsXLA (Alpha 5.0) 2009.Nov.21.(17.25)	

BugsXLA is provided without any warranty of any kind, eith
The user is responsible for any consequences arising from
See also the disclaimer provided with the WinBUGS packa

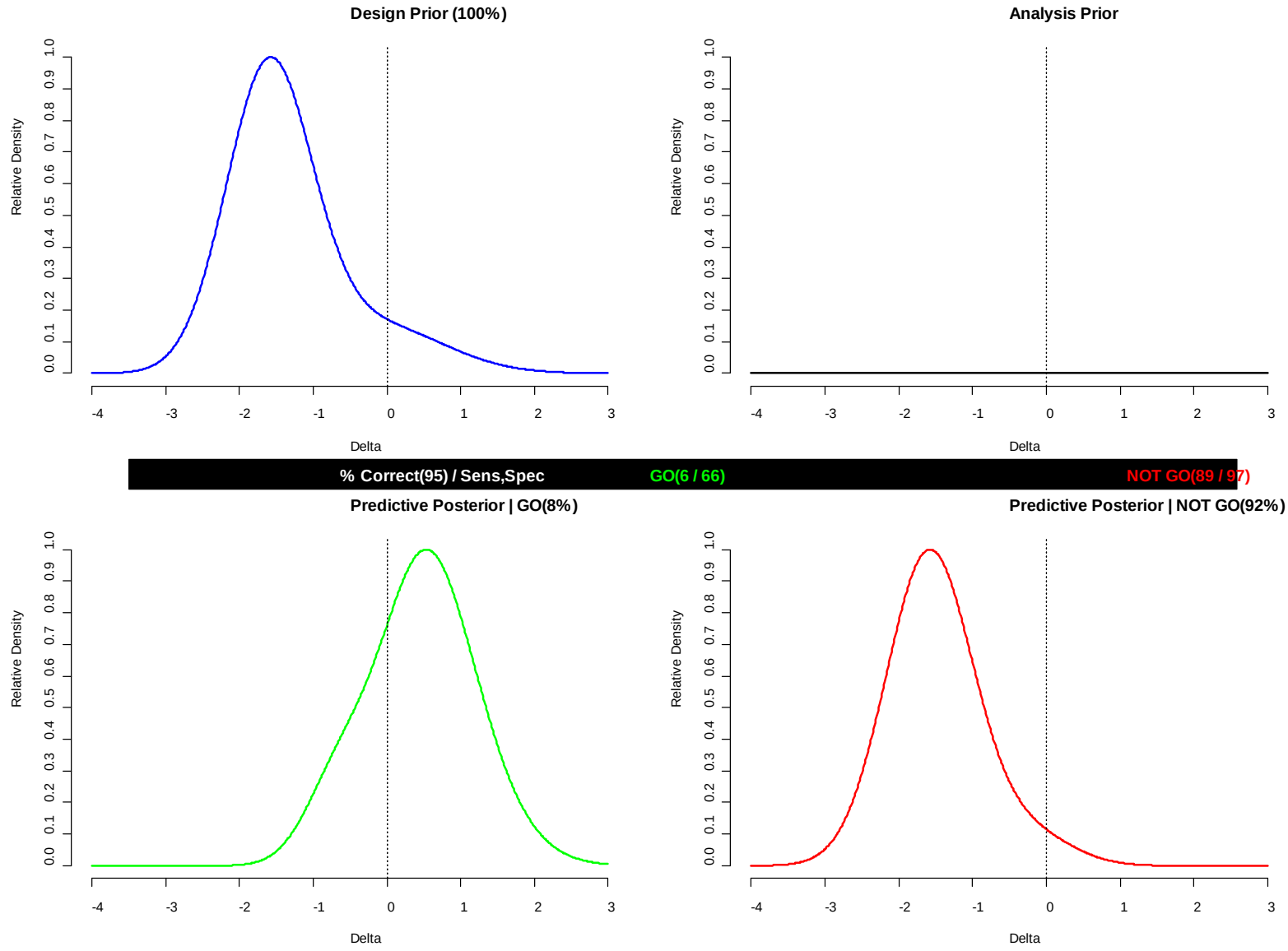
Elicited Prior Distribution (Novel Treatment)



Study OC with Prior Overlaid



Positive & Negative Predictive Distributions



Interim Analysis

Stop for futility

Probability of STOP at study end < 20%.

Stop for clear efficacy

Probability of GO at study end > 80%.

Continue otherwise.

Final Thoughts

Education & training in Bayesian approach

Most statisticians need support

both technically & in leading change

Concepts not an issue for non-statisticians

more intuitive than frequentist methods

Final Thoughts

More general resistance to change

- Current dissatisfaction > Anxiety due to managing resistance
- Must be a vocal and passionate advocate
  - Strong communicator & influencer
  - Challenge the status quo
  - Be assertive
- Maintain a consistent core set of beliefs ...
  ... but be prepared to learn as you go
  - Focus on what adds most value to the Business
    e.g. Bayes prior reduces N leading to quicker & cheaper studies
- Make allies in partner lines
  - Build strong relationships across the Business

Final Thoughts

A leader is only as good as the people in his team

Peter Colman

Dave Collins

Susie Collins

Kat Gore

Frances Hackman

Ieu Jones

Nathalie Massat

Alison McLeod

Trevor Smart

Phil Stanley

Bernie Surujbally

Ros Walley