An Examination of Risk & Outcomes in Outsourcing

A Case Study To Help You Consider Your Options

19 May, 2015

Steve Herbert
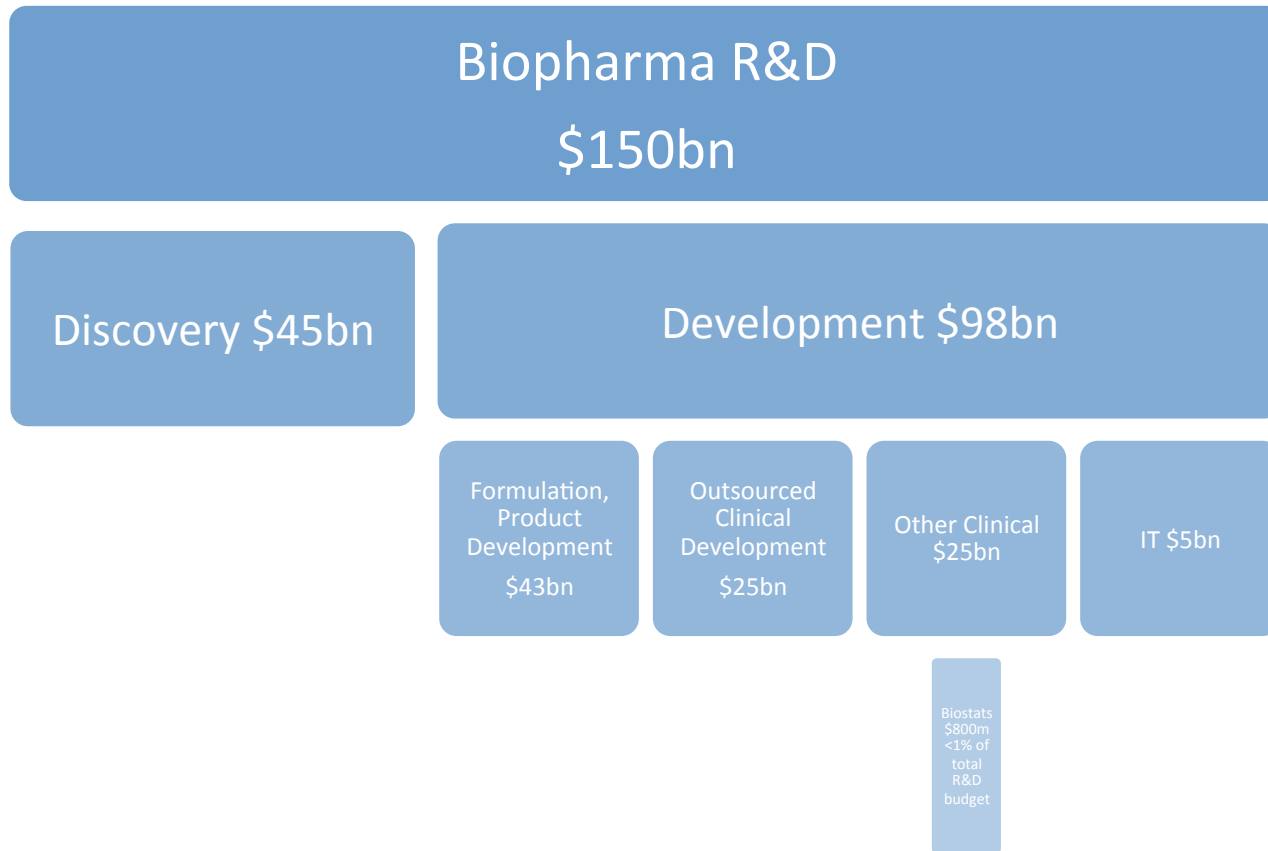**Senior Vice President, Cytel Inc.**

What You Will Learn

A coherent way to categorize risk in the context of pharmaceutical development

How outsourcing can effect risk, cost & outcome in both good and bad ways

Why you need to pay closer attention to your biostats & data management provider

How to use outsourcing to reduce risk

$25bn Outsourced: Clinical Development

Biopharma R&D

$150bn

Discovery $45bn

Development $98bn

Formulation, Product Development $43bn

Outsourced Clinical Development $25bn

Other Clinical $25bn
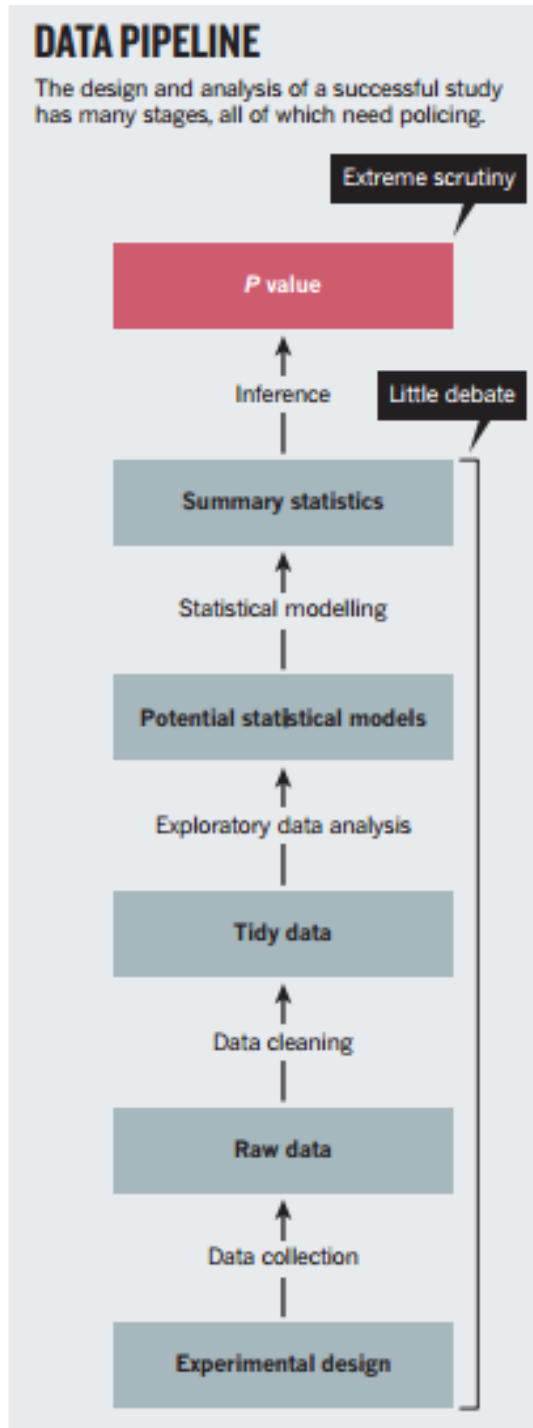
IT $5bn

Biostats $800m <1% of total R&D budget

Why a great biostats & data management provider is important

"Ridding science of shoddy statistics will require scrutiny of every step, not merely the last one,"

Jeffrey T. Leek and Roger D. Peng, Associate professors of biostatistics at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, USA.

DATA PIPELINE

The design and analysis of a successful study has many stages, all of which need policing.

Extreme scrutiny

P value

↑ Inference   Little debate

Summary statistics

↑ Statistical modelling

Potential statistical models

↑ Exploratory data analysis

Tidy data

↑ Data cleaning

Raw data

↑ Data collection

Experimental design

Risk: A Definition

RISK

The possibility that something bad or unpleasant will happen

Such as an injury or loss

© Webster

Risk
categories in drug development

Technical — Efficacy and Safety profiles

- The unknown outcome of the trial
- NCE safety profile

Regulatory — Uncertainty of approvability

- Changing and challenging regulatory environment

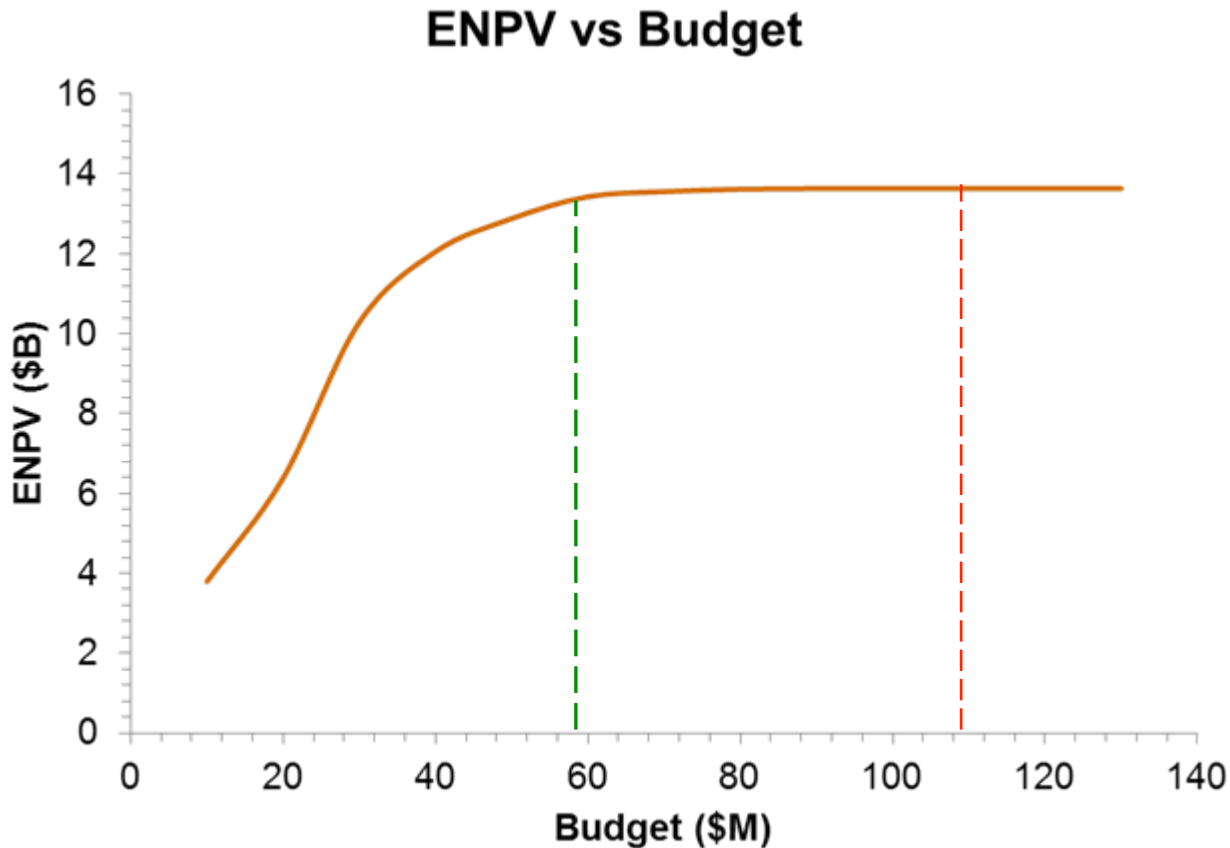**Commercial** — Assumptions affecting ROI over life of therapy

- Uncertain reimbursement prospects
- Competitive risk from new therapies
- Managing the expiration of exclusivity

Decision — Assumptions & Design Decisions

- Efficacy, target population, end-point & other protocol assumptions of trial
- Investment decisions
- Timing assumptions of trial end etc.

98% of the return : 50% of the Investment

ENPV vs Budget

Dynamically Optimizing Budget Allocation for Phase 3 Drug Development Portfolios Incorporating Uncertainty in the Pipeline, Patel & Ankolekar, 2015

Statistical risk is not what we perceive as risky

It turns out that walking or going downstairs is more risky than whitewater kayaking …

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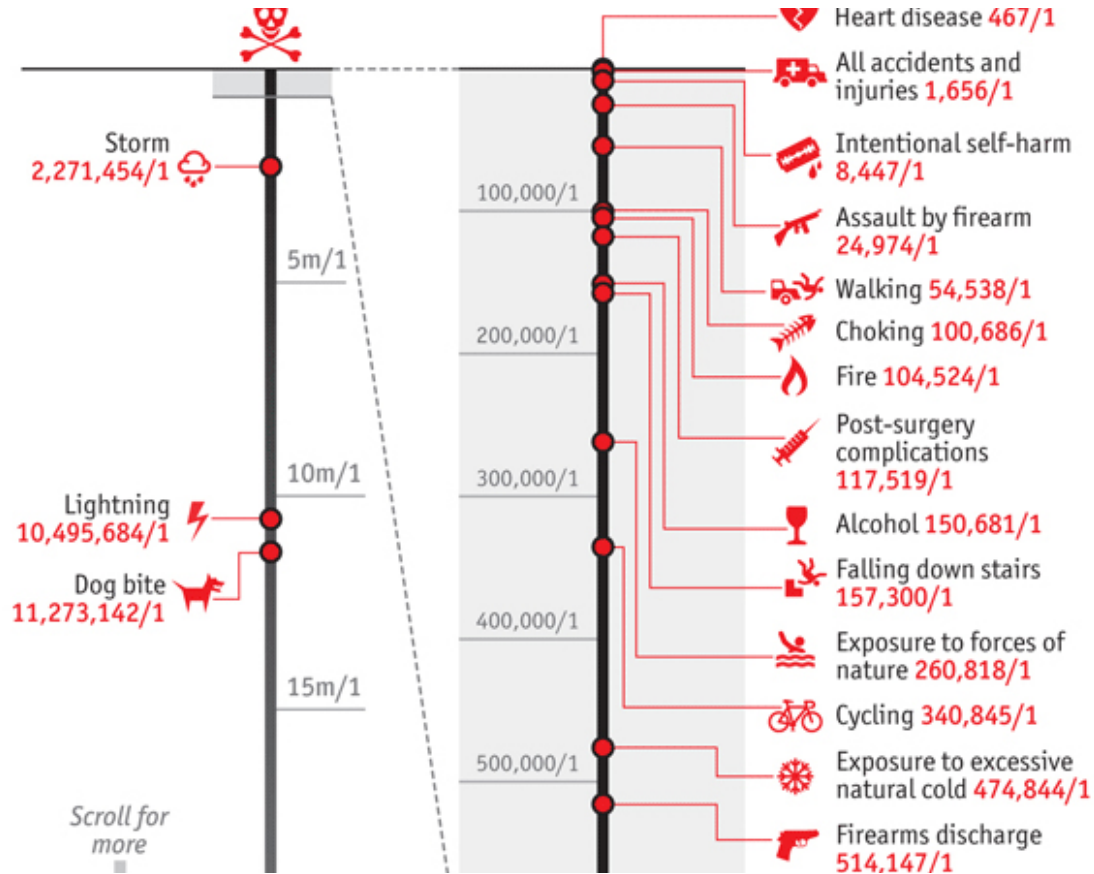
Statistical risk is not what we perceive as risky

You need a team who can help you perform data analysis in the real world. Realize that some circumstances set them up for success, and some for failure …

© The Economist, Danger of death! Feb 14th 2013

To Mitigate Risk you have to Know its Source

Unpredictable fluctuations

- You don't know when patients will arrive nor when events will occur
- You don't know how to staff in preparation for a study or program because the timing, and potentially sizing and progress are unknown

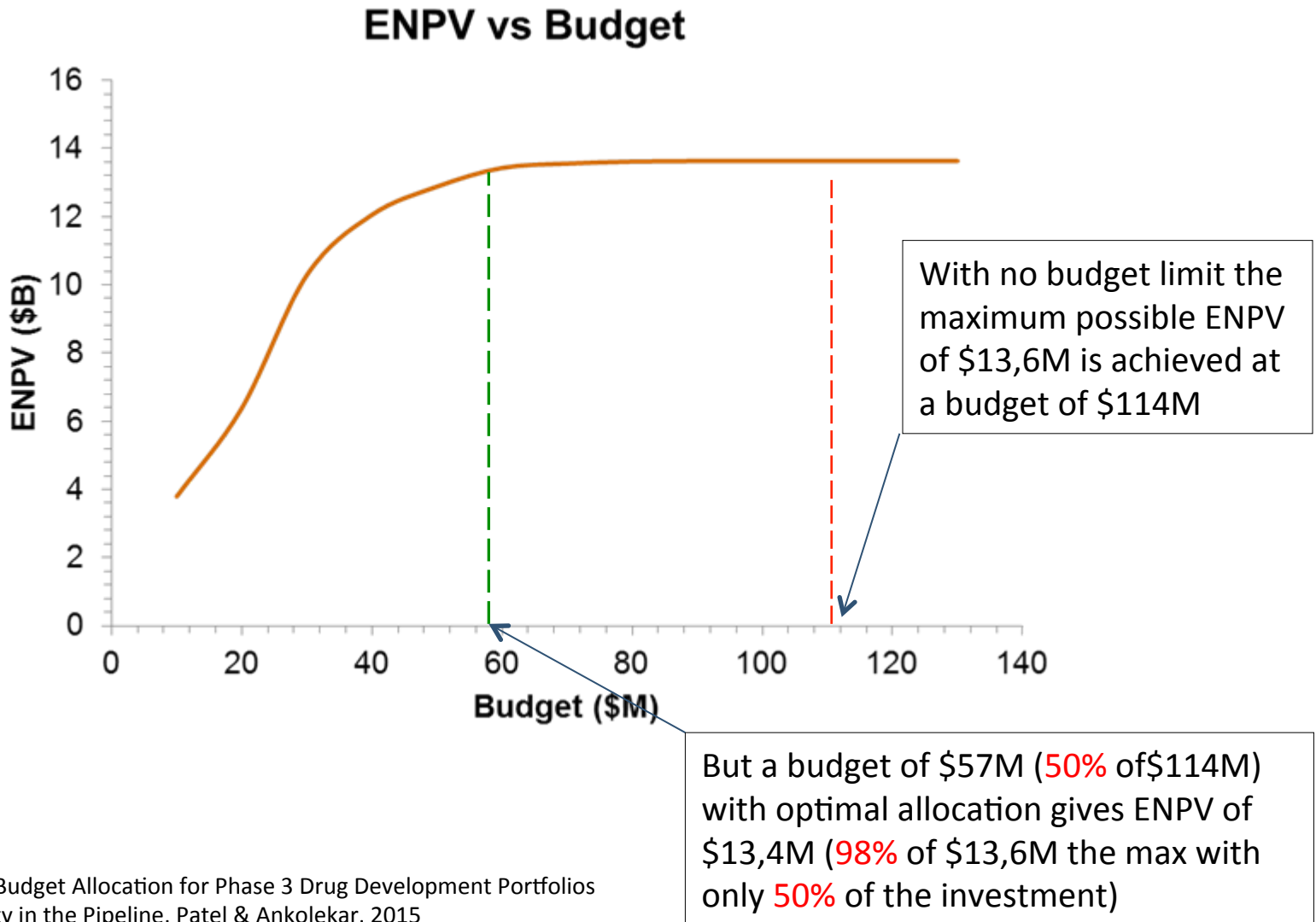## Peak flows which are large multiples of normal workload

- When a big study gets going you need all hands on deck when you need them. If another big study does not immediately follow, you have a lot of heads and hands standing around twiddling their thumbs
- You need staffing staged to provide biostats & programmers at the beginning, clinical research associates during the enrolment, data managers, clinicians etc. each at the right time

Assumptions about unknowns

- The study protocol itself: probably embodies the major sources of risk in any clinical study in its implicit and explicit assumptions about unknowns such as effect size, enrolment rates, and event rates for example.
- Marketing assumptions probably are the other largest source of risk: market size, ROI, competition

Assessment of risk from a too narrow or static point of view

98% of the return : 50% of the Investment

ENPV vs Budget

With no budget limit the maximum possible ENPV of $13,6M is achieved at a budget of $114M

But a budget of $57M (50% of$114M) with optimal allocation gives ENPV of $13,4M (98% of $13,6M the max with only 50% of the investment)
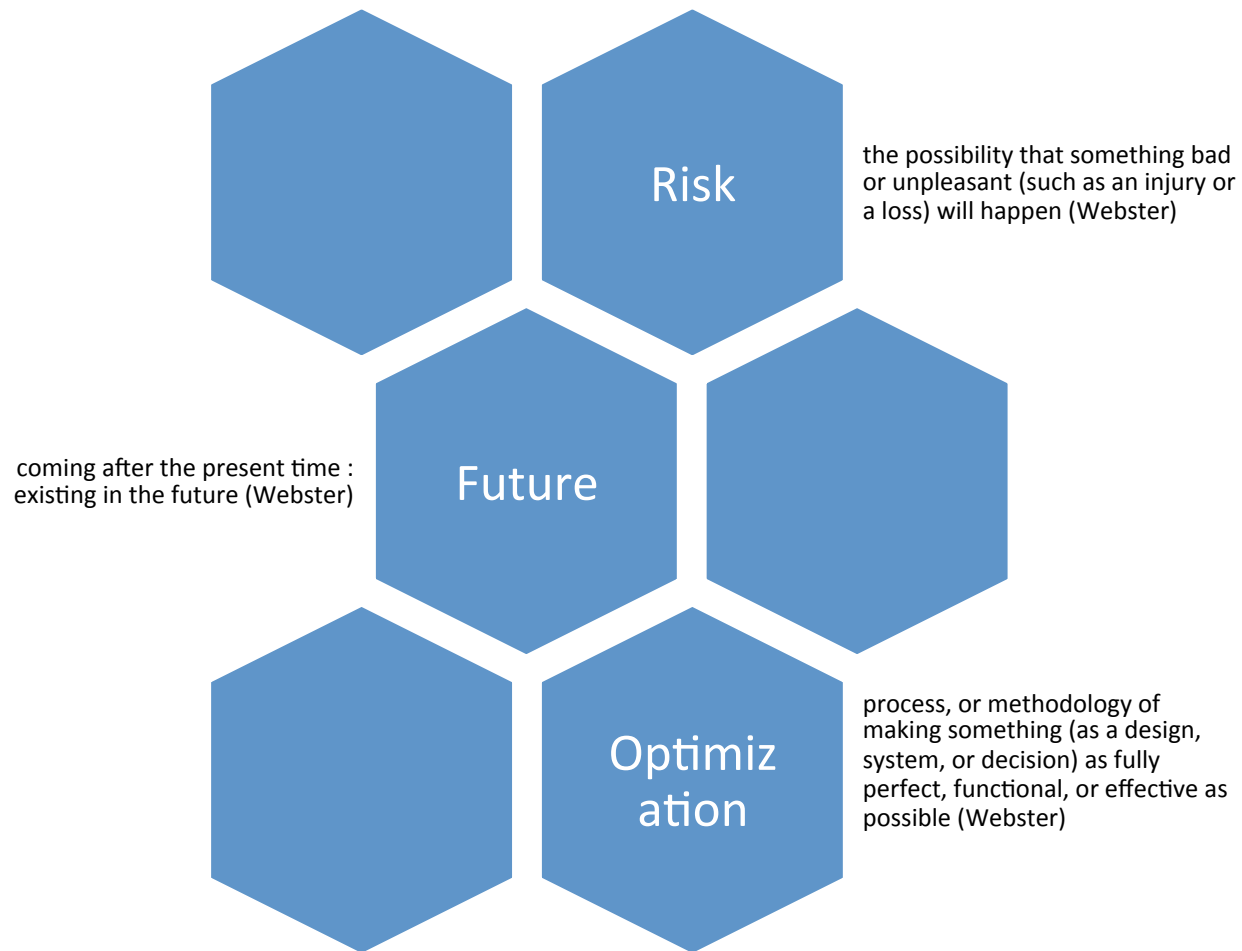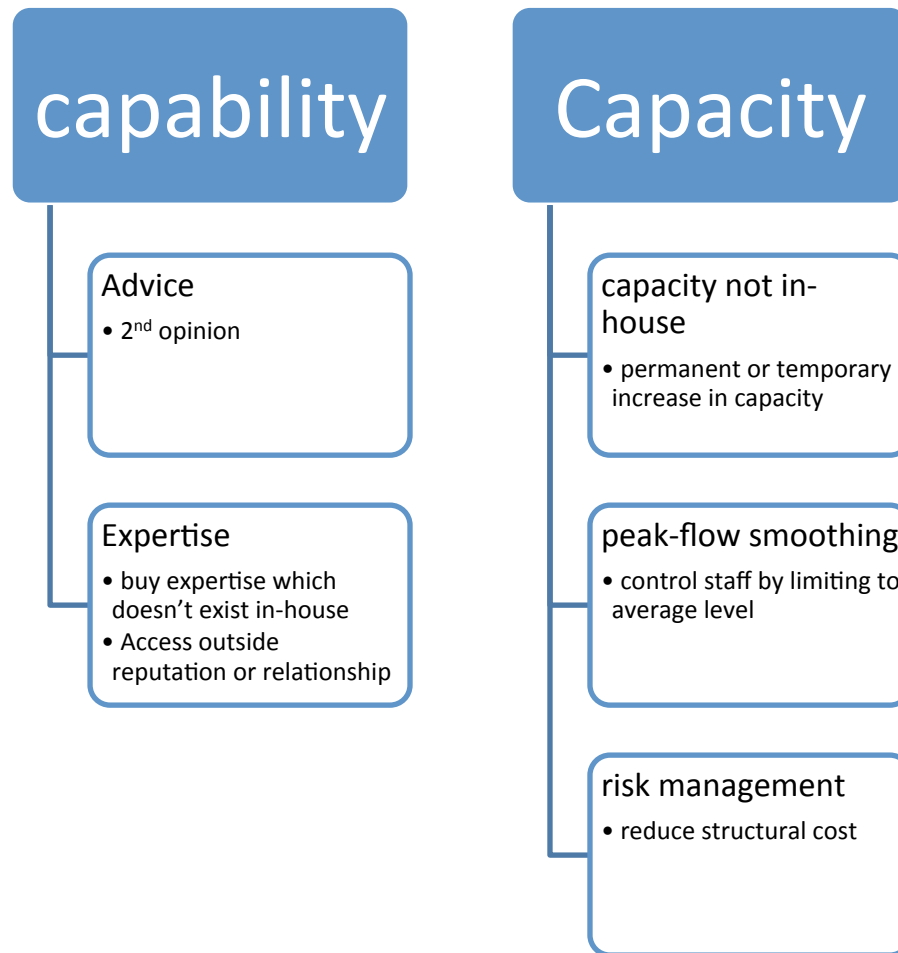
Computer-Assisted Decision-Making

Input Potential True Values; Compute Operating Characerics for
Decision Rules (Probability of Go / NoGo / "need further assessment")

Risk
Simulating & Optimizing the Future

Risk — the possibility that something bad or unpleasant (such as an injury or a loss) will happen (Webster)

Future — coming after the present time : existing in the future (Webster)

Optimization — process, or methodology of making something (as a design, system, or decision) as fully perfect, functional, or effective as possible (Webster)

Outsourcing: A Definition

capability

Advice
- 2nd opinion

Expertise
- buy expertise which doesn't exist in-house
- Access outside reputation or relationship

Capacity

capacity not in-house
- permanent or temporary increase in capacity

peak-flow smoothing
- control staff by limiting to average level

risk management
- reduce structural cost

Why do sponsors actually say they outsource?

1. Reduced costs (53%)
2. Improved quality (43%)
3. Improved efficiency in use of internal staff (43%)
4. Access to operational expertise (43%)
5. Process improvement (30%)[1]

[1] Avoca: Strategic Partnerships Under Scrutiny: Are They Working and How Long Does It Take? Executive Summary of The Avoca Group's 2012 Industry Survey Research,
http://www2.theavocagroup.com/content/documents/files/Executive_Summary_-_2012_Industry_Survey.pdf

What do sponsors think after they've tried it?

59% of sponsors said after 3yrs they were getting worse quality than in-house [1]

[1] Avoca Consortium of Quality, Quality Summit Report, 2012,
http://www2.theavocagroup.com/the-avoca-quality-consortium/consortium-news-and-updates/the-avoca-2012-quality-summit-report

Quality is a constant companion of outsourcing

Rework and quality: 22% of sponsor companies surveyed by Avoca reported having discontinued strategic relationships ... because of poor quality of deliverables, http://www2.theavocagroup.com/

[1] Avoca Consortium of Quality, Quality Summit Report, 2012, http://www2.theavocagroup.com/the-avoca-quality-consortium/consortium-news-and-updates/the-avoca-2012-quality-summit-report

A Specialty BDM provider

"… education is not enough. Data analysis is taught through an apprenticeship model, and different disciplines develop their own analysis subcultures. Decisions are based on cultural conventions in specific communities rather than on empirical evidence.

For example, economists call data measured over time 'panel data', to which they frequently apply mixed-effects models. Biomedical scientists refer to the same type of data structure as 'longitudinal data', and often go at it with generalized estimating equations."

References & Credits

Peter Lord, for inspiration and humour

Dr Nitin Patel, Zoran Antonijevic, Jim Bolognese, Yannis Jemiai & Mike Weitz: for guidance in the preparation and for specific slides on ENPV

Danger of death! Feb 14th 2013, 18:27 BY ECONOMIST.COM

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VALOR, Sunesis (promising zone adaptive trial, met secondary end point); ADVENT, Fuluzaq, Napo Pharmaceuticals (seamless dose finding-III, approved 2013). Procysbi, Raptor (SSR, Rare disease approved 2014)

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Go No-Go v1.0: User Guide Charles Liu, Jim Bolognese, Jaydeep Bhattacharyya, Nitin Patel, 2012, Cytel, Inc.

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SCRUM: The Art of Doing Twice the Work in Half the Time, Jeff Sutherland, co-creator of Scrum, 2014, Crown Business Publications
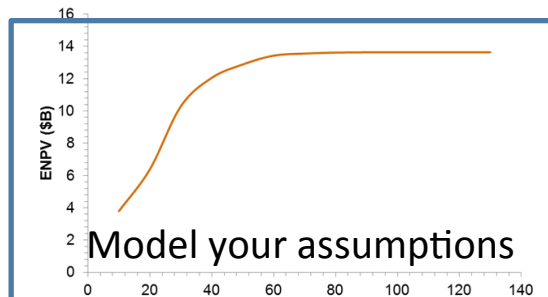
Summary

Use specialized providers

Quality before Price

OUTSOURCE

Question your statistics

Model your assumptions

Outsource for workload flexibility

Where you can get these slides

www.cytel.com

How can you get in touch with me

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Thank you.

Your comments or questions?

19 May 2015
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