Statisticians in the Pharmaceutical Industry: The 21st Century

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Outline

- Evolving role of statisticians
- Core competencies of statisticians
- The external environment
- Responses to the changes in the environment
- Develop partnerships and collaborations
- Examples of collaborations
- Fostering innovations
- Our future

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Evolving Role of Statistics

Little use of Statistics ==>

"Required" use of Clin Statistics ==>

Tactical use of Statistics ==>

Strategic use of Statistics & "Statistical Thinking"

1955 2008 and beyond

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Industry Perspective: "Then"

- Hired some statisticians to get things through the regulatory agency (mostly in the US)
- "Number crunchers" to get analyses done
- "Blessed" clinical trial designs with minimal intellectual participation except sample size
- Clinical and manufacturing focus
- Very little input outside of "necessary", low involvement in non-clinical areas
- Statisticians played a secondary role

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Statistician's Role: Now and the Future

- Full and equal partner with basic, clinical & regulatory scientists as articulated in the ICH-E9 document.
- Focus on experimental design *and* development strategy.
- Application of statistical thinking throughout the life cycle of a pharmaceutical product.
- Statisticians solve problems differently from other scientists, adding important diversity to the scientific debate.
- Parallel development in other disciplines such as epidemiology, genomics, biomarker development, and risk management expands statistician's contributions.

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Why the Change?

- Information is the capital, not just numbers
- Champions for quantitative decisions
- Statisticians successfully taking on different roles
- Drug development has become more complex
- Learned collaborators and consumers demanding more information
- Statistician as effective teacher and communicator
- Statistician with expanded skill sets

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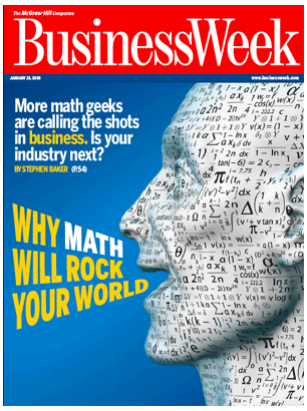
Why Math Rules?

23 Jan 2006



"As more of the world's information is pooled into mathematics, the realm of numbers becomes an ever larger meeting ground. It's a percolating laboratory full of surprising connections, and a birthplace for new industries. Yes, it's a magnificent time to know math."

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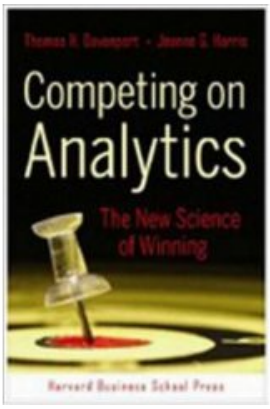
Competing on Analytics

Jan 2007



"The growth of analytical competition will lead to a need for substantially greater numbers of analytically oriented people."

The Winning Formula

"If it is worth doing, it is worth doing *analytically*."

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Competency: Statisticians

- Skill, capability, and characteristics
  - Technical knowledge (e.g. design, analysis, modeling)
  - Computing (e.g. simulations)
  - Non-quantitative learning (e.g. biology, regulations)
  - Identifying, formulating and solving problems
  - Communication
  - Collaboration and team work
  - Leadership
- Emphasis associated with each competency depends on the specific job responsibility

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Statisticians in Pharma Industry

- Being technically smart is not enough:
  - Understand the broad clinical, regulatory and public-health context
  - Communicate statistical strengths and weaknesses
- Proactive, not passive:
  - Design: Options available, decision analysis
  - Execution: Quality control and risk mitigation
  - Analysis: Planned and unplanned, strengths/weaknesses
  - Interpretation: Pre-planned or data-driven
  - Presentations/Publications: Keeping audience in mind.

Statistics is a Collaborative Science!!

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Organizational Support

- Mentorship
- Role models
- Culture of continuous learning
- Make operational aspects of reporting a non-issue
- The statistics function itself, should not become the objective

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The External Environment

- Desire for more transparency in clinical research and clinical reporting
- A perceived need for more public “control” over the search for valuable medicines
- Loss of public confidence in the clinical research process and the pharmaceutical industry
- Loss of public confidence in the regulators
- An increasing demand for product safety

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What Happens?

Have we wandered away from our patient-based mission?

We need to return to being more a science based enterprise.

We need to manage the many more stakeholders more effectively.

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Our External Stakeholders

- Health care providers
- Patient care givers
- Regulators
- Journal editors
- Shareholders
- Health care payer
- And most importantly - **THE PATIENTS**

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Data Disclosure

- Desire for more “transparency” in the clinical research process
  - ICMJE, IOM, WHO, NLM
  - Protocols
  - Results
  - Logistics
- JAMA Policy
- “Conflict of interest”
- US FDAAA law

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Responses

- Registries
- Meetings and Journal Discussions (many)
- Publications and editorials
  - BMJ
  - IBS
  - JASA
  - J of Pharmaceutical Statistics
  - Biopharm report

We routinely submit protocols, data and reports to multiple regulatory agencies.

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How can the Statistician Help?

- Leverage the drive for transparency.
- Cultivate collaboration within the teams and within the statistics function.
- Develop partnerships with academia and government.

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Leverage the Drive for Transparency

- Improve study designs
  - All studies will be public and designs will be subject to public scrutiny.
- Improve communication
  - Provide informative displays and presentations of results that are customized for the audience.
- Endorse the use of common standards
  - Maximize the efficiency of collecting and sharing data via the use of common standards.

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Develop Partnerships

- Foster partnerships among academia, industry and government.
- Reasons:
  - Solve complex problems by sharing resources and knowledge
  - Integrate ideas and increase credibility through peer review
  - Create solutions to account for differing perspectives
- Belief:
  - Working together is more effective than working in isolation

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Partnership Models

- Consultative:
  - Gather input to inform future strategic direction
- Contributory:
  - Formed to benefit the work of one of the partners
- Operational:
  - Set strategic direction with implementation by one of the partners
- Collaborative:
  - Share resources, risks and decision making
  - Share open source software

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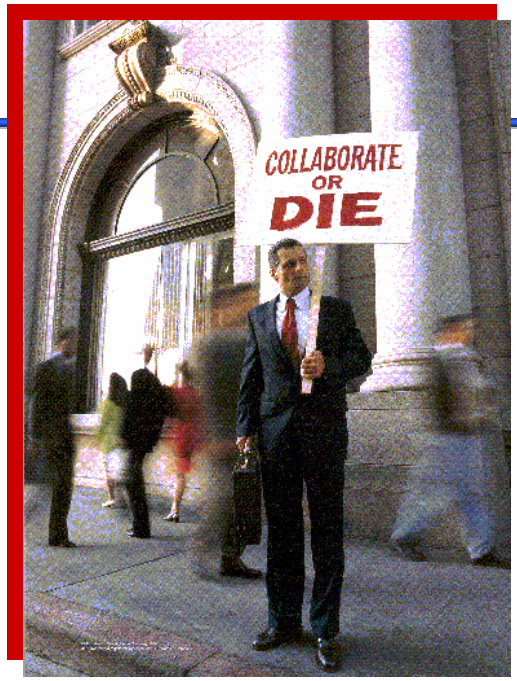

Source:
A.G. Edwards advertisement

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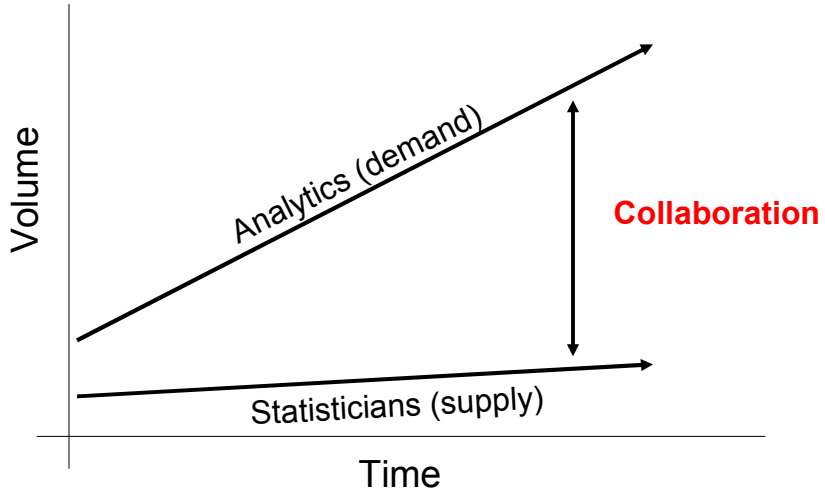
Filling the Analytics Gap



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ASA Created the SPAIG Award

- SPAIG: Statistical Partnerships among Academe, Industry and Government
  - SPAIG Committee Charge: Identify, lead and promote initiatives that foster partnerships among academia, industry and government.
  - SPAIG Committee Award: Established in 2002 to recognize outstanding partnerships established between academe, industry and government organizations and to promote new partnerships. Award recognizes organizations; not individuals.
  - For more information, go to www.amstat.org and then "Committee".

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Adaptive Designs

PhRMA Definition

- uses accumulating data to decide on how to modify aspects of the study
- without undermining the *validity* and *integrity* of the trial

ADWG: Adaptive Design Working Group

Validity means

- providing correct statistical inference (such as adjusted p-values, estimates and confidence intervals)
- assuring consistency between different stages of the study
- minimizing operational bias

Integrity means

- providing convincing results to a broader scientific community
- preplanning, as much as possible, based on intended adaptations
- maintaining confidentiality of data

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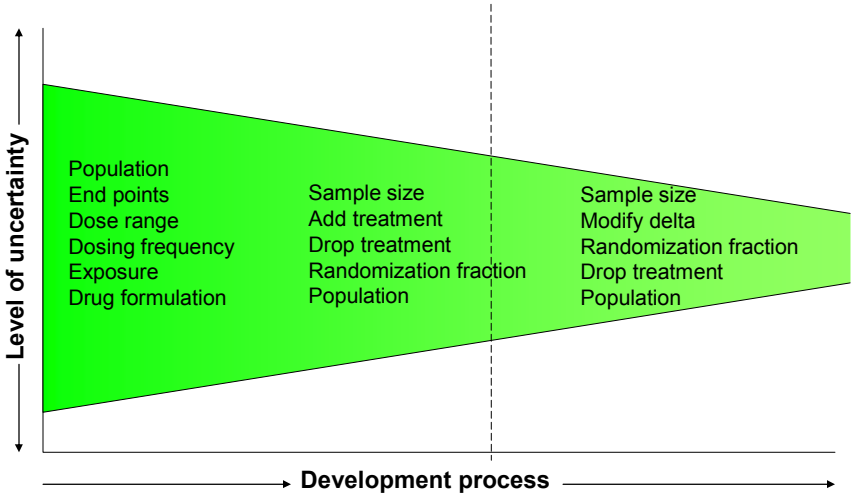
Drug Development Process



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ADWG: History and Milestones

- ADWG was formed in 2005, consisting of academic and industry members.
- It helped organize PhRMA's workshop on adaptive designs in 2006.
- ADWG published 8 papers, 2 more accepted, numerous under preparation.
- ADWG met ftf 6 times. The most recent one took place on April 3rd 2008.
- In 2007, ADWG initiated 9 workstreams to focus on education, implementation, and global harmonization.
- ADWG has active US and European members. It has recently connected with EFPIA and JPMA in Japan.
- ADWG is driving a global agenda.

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9 Workstreams of ADWG

- Education Effort
- ICH harmonization
- Data monitoring issues and processes
- Good adaptive practices
- Case studies to share experience
- Software user requirements
- Material manufacturing and supply
- Communications
- Key Opinion Leader lecture series

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Regulatory Interactions

- A core group of ADWG met with FDA senior management members, August 14 2007.
- ADWG participated in an EMEA/EFPIA workshop on adaptive designs in confirmatory trials in London, Dec 14 2007.
- The Case Studies workstream shared case studies at an FDA training event on April 2 2008.
- The Communications workstream provided seminars to staff at Health Canada, April 29-30 2008.
- Discussion is ongoing between EMEA/EFPIA to hold another EMEA/EFPIA workshop to look at implementation.
- Work with the JPMA Interim Analysis Task Force to create opportunities to meet with PMDA in Japan.

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Other Examples of Collaborations

- QT Effect of a Pharmaceutical Product
- Multiple Co-primary Endpoints
- Active Control Study
- Methods to Handle Missing Data
- Dichotomizing Continuous Endpoint
- Biomarker Quantification
- Predictive Model (Pre-clinical to Clinical)
- Safety Data Evaluation
- Global Trials
- Other FDA *Critical Path* Opportunities

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Innovations and FDA Critical Path Initiative

Innovations: the vital spark of all human change, improvement and progress.

Innovations include new methods or innovative applications of existing methods.

Critical Path is the FDA's premier initiative to identify and prioritize the most pressing medical product development problems and the greatest opportunities for rapid improvement in public health benefits.

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Fostering Innovation

- Innovation can occur at the team level, organizational level (within-company), cross-organizational level (industry-wide collaborations), cross-area level (industry-academia collaborations).
- Innovation is often within the ability of every practicing statistician.
- Collaborations are very powerful means to drive positive changes, but the sparks of innovation need to start and be nurtured from within.

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Factors Contributing to Success

- Vision and strategy
- Driving innovation requires a holistic approach
  - Within company as well as in the external community (e.g., industry partners, academia, Health Authorities, medical community)
- Strong champions
- Culture for recognizing scientific advancements at multiple levels
- Opportunities to highlight value added
  - Opportunities & platform to discuss with senior management

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Factors Contributing to Success (2)

- Awareness of business consulting environment
  - Can use business consultant feedback to senior management to leverage innovation capabilities
- Strong capabilities to implement, including
  - Strategic/tactical perspective and proactivity
  - Broad and strong technical/leadership skills
  - Excellent communciation skills
  - Strong collaboration, influencing and facilitation skills
  - Strong problem-solving skills
- Strong credibility of the innovating statisticians in the internal and external community

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Change is not essential…

survival is not mandatory

W. Edwards Deming

Nobel Laureate, Economics

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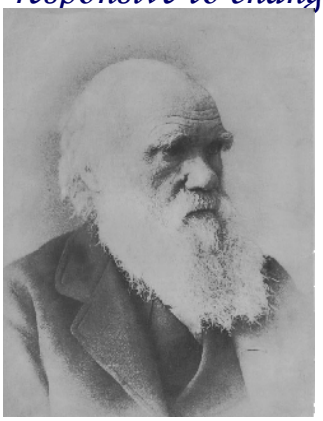
It is not the strongest of the species that survive, nor the most intelligent, but the one most responsive to change.



Charles Darwin
On the Origin of Species*
1859

*On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life.

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"The future ain't what it used to be!"

Yogi Berra
Former All-Star Catcher
New York Yankees

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Our Future

- Just as energy is the basis of life itself, and ideas the source of innovation, so is innovation the vital spark of all human change, improvement and progress.
  – Theodore Levitt
- Most people have a desire to look at the exception instead of the desire to become exceptional. - John C. Maxwell
- The great thing in this world is not so much where we stand, as in what direction we are moving.
  – Oliver Wendell Holmes
- Opportunities are aplenty; so are our responsibilities to take advantage of them.
- **Get Ready!**

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