

# Using Web-based Systematic Reviews for More Effective Clinical Research

**Peter O'Brien**



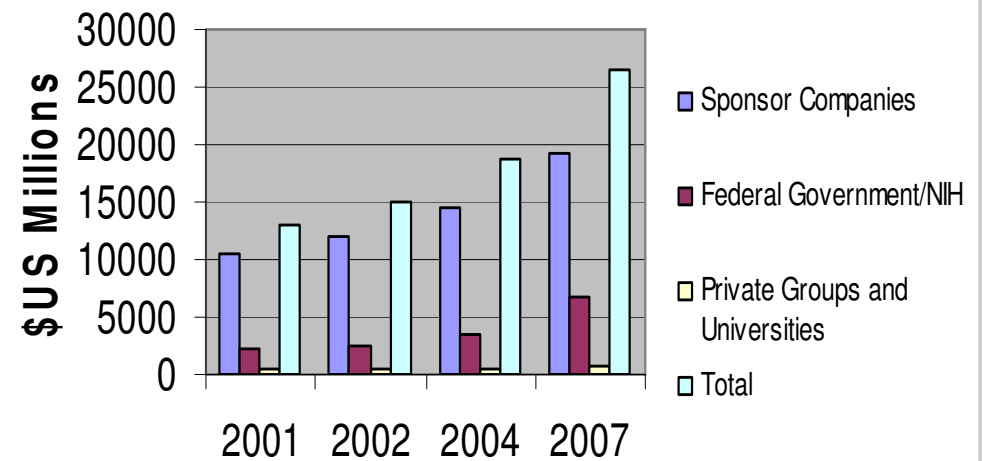
- **Primary Research Challenges**
- **The Promise of Systematic Reviews**
- **Web-Based Systematic Reviews**
- **Benefits and Issues**
- **The Clinical Trials EDC Adoption Analogy**
- **What's Next**
- **Discussion/Experiences**



# Primary Research

- **Costly**
  - The average phase 3 clinical trial costs roughly \$100 million US
  - Time from patent to market carries opportunity cost of up to \$1 million per day
- **Multiple Trials Often Needed**
  - How many trials are required to prove safety and efficacy

## Sources of Trial Funding



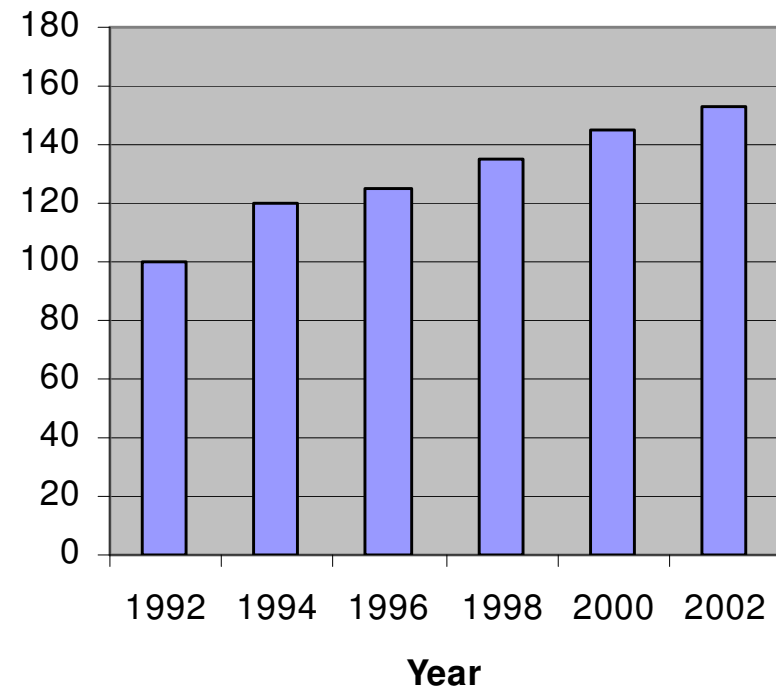
Source: Thomson CenterWatch Analysis, 2004



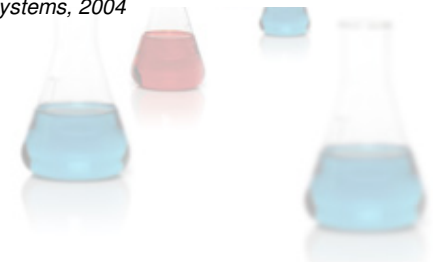
# Primary Research

- **Experimenting on Humans**
  - Risk
  - Ethical Issues
  - Adherence and follow up
- **Regulatory Overhead**
  - FDA, EMEA, Heath Canada, HIPAA, PIPEDA

**Mean Number of Procedures per Patient**

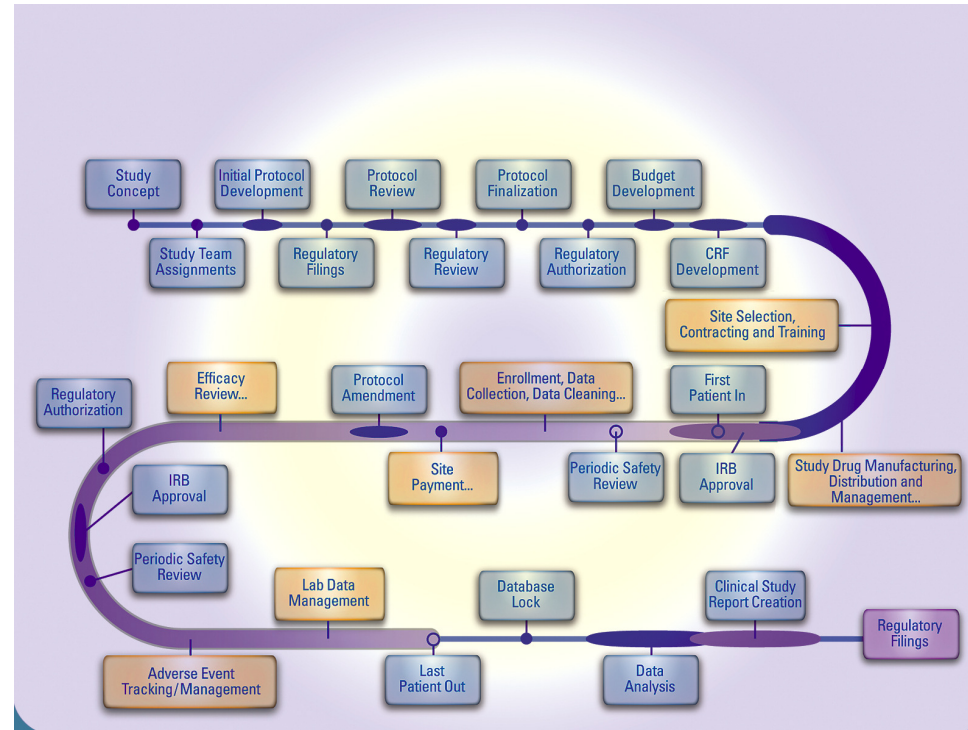


Source: Thomson CenterWatch Analysis, 2004; Parexcel Sourcebook, 2004-2005; Fast Track Systems, 2004



# What Clinical Research Needs to Be

- **Safer**
  - Minimize patient risk and exposure through the research process
- **Better**
  - More statistically significant results
- **Faster**
  - Time to prove or disprove an idea reduced
- **Cheaper**
  - Getting more bang for our research dollar



Clinical Trial Life Cycle



# Why Systematic Reviews in Clinical Research?

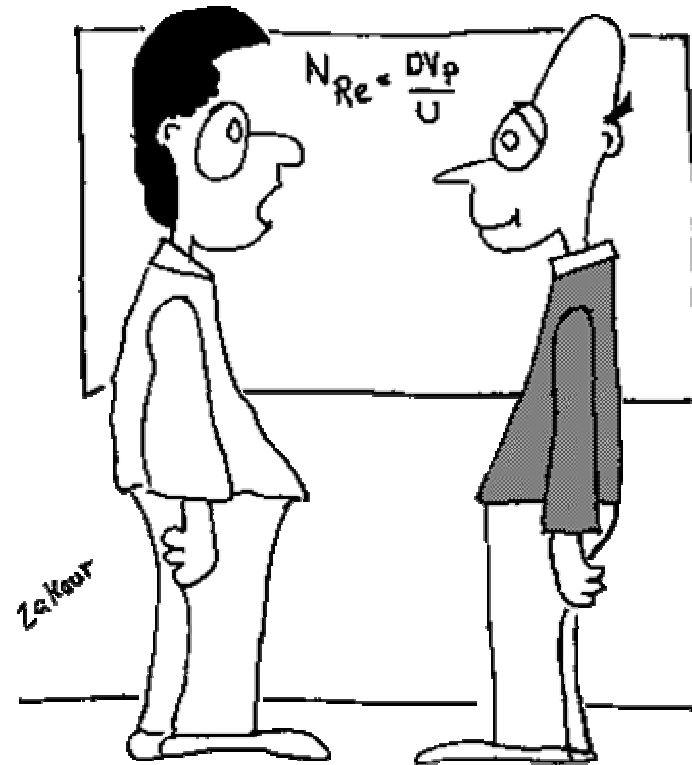
- **More Ethical Clinical Trials**
  - **Systematic reviews to inform trial design\***
    - Prevent unneeded trials OR prove that a trial is needed
    - Potentially reduce size, duration and number of procedures in a trial
  - **Systematic reviews to interpret trial results\***
- **Less Regulatory Overhead than Trials**
- **Generally faster**
  - **Months vs Years**



\* Doug Altman The Ethical Requirement for Systematic Reviews for Randomized Trials, *Principles of Health Care Ethics, Second Edition* 697-701

# Why Systematic Reviews in Clinical Research?

- **Cost**
  - Reviews allow trial designs to be more efficient
    - Fewer patients
    - Fewer interventions
    - Reduced time frames
  - In academic research reviews may cost 1/150 of clinical trial costs\*
- **Quality**
  - How many trials are needed to prove safety and efficacy



After years of extensive research, I have concluded beyond any doubt that I need more grants!

\* Paul Glasziou, Ben Djulbegovic, Amanda Burlis **Are systematic reviews more cost-effective than randomized trials?** The Lancet\_Vol 367 June 24, 2006

# Systematic Review Challenges

- **Often poorly funded**
  - Volunteer/unofficial team members, limited resources
- **Finite shelf life<sup>1</sup>**
- **Operationally challenging**
  - Large volume of paper and information
  - Synchronizing input from multiple participants
- **Remote Experts**
  - Subject matter expertise may not be local
- **Not always transparent**
  - Raw and source data may not be easily accessible internally or to third parties
- **Error prone<sup>2</sup>**
  - Transcription/data entry errors<sup>3</sup>
  - Manual decision errors

Reality



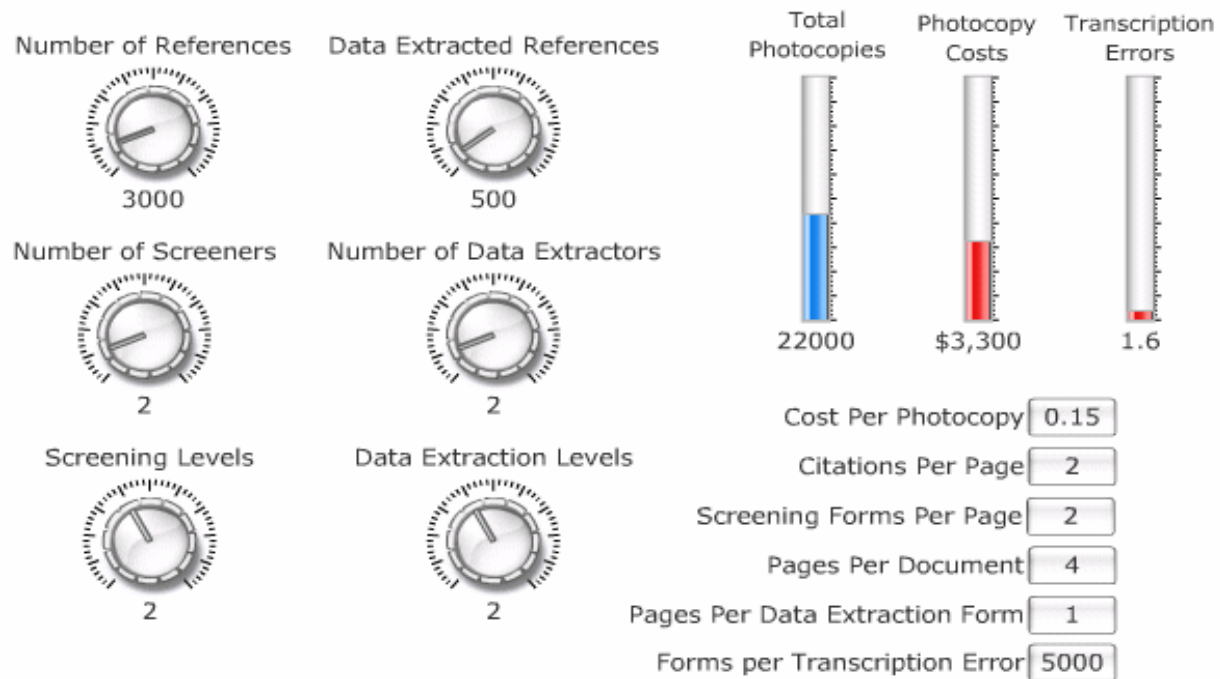
1. Kaveh G. Shojania, MD; Margaret Sampson, MLIS; Mohammed T. Ansari, MBBS, MMedSc, MPhil; Jun Ji, MD, MHA; Steve Doucette, MSc; and David Moher, PhD How Quickly Do Systematic Reviews Go Out of Date? A Survival Analysis Annals of Internal Medicine **21 August 2007, Volume 147 Issue 4, Pages 224-233**

2. Eysenbach G, Kummervold PE "Is Cybermedicine Killing You?" - The Story of a Cochrane Disaster J Med Internet Res 2005;7(2):e21

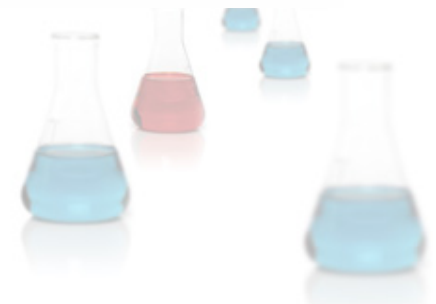
3. **Morris L Rivera**<sup>1,2</sup>, **Jason Donnelly**<sup>2</sup>, **Blair A Parry**<sup>2</sup>, **Anthony Dinizio**<sup>2</sup>, **Charles L Johnson**<sup>3</sup>, **Jeffrey A Kline**<sup>4</sup> and **Christopher Kabrhel**<sup>2</sup> Prospective, randomized evaluation of a personal digital assistant-based research tool in the emergency department BioMed Central Medical Informatics and Decision Making January 2008

# Paper in Traditional Reviews

- Paper = time, errors, cost and overhead



Copyright TrialStat Corporation 2004



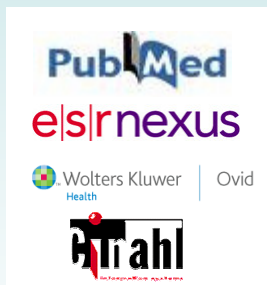
# Definition of a Web-Based Systematic Review

- **Collaborative, multi-user system**
- **Centralized database for screening and data abstraction data**
- **Interface is web browser-based**
- **Online reference and document storage**
- **Electronic screening and data extraction forms**
- **Automated collation, validation and processing**
  - **Reviewer conflict checking**
  - **Reference Inclusion/Exclusion**
- **Real-time reporting and monitoring**
- **Data querying and export**



# Web-Based Systematic Reviews

## Reference Search



## Organize Results



## Web-Based Portion of the Review

- Form/protocol authoring
- Article de-duplication
- Global Reviewer Collaboration
  - Screening
  - Coding
  - Data abstraction
- Process Automation
  - Inclusion/exclusion
  - Conflict detection
- Real time reporting
- Team, work flow and data management

( Manual/paper-based process  
in traditional Systematic Reviews )

## Analyze and Format Data



## Publish or File



# Why Web-Based Reviews

- **Enhanced collaboration**
  - Real-time, multi-user participation
  - Geographically agnostic
  - Enhances Adaptive Protocol Change Capabilities
- **Improved data quality**
  - No transcription
  - Collation, conflict checks and inclusion/exclusion of references are automated
- **Fully transparent, auditable and reproducible process**
  - All transactions logged with names and timestamps
  - Zero data or source material loss
  - Raw data can be easily pushed to the web for scrutiny



# Why Web-Based Reviews

- **Cost savings**
  - **Printing and distribution of abstracts, references and study instruments eliminated**
  - **No transcription costs**
  - **Reduced communication costs for geographically distributed reviews**
    - **Phone, travel, post**
- **Reduced carbon footprint**
  - **Dramatic reduction in paper and transportation usage**
- **Ethics?**
  - **We should used the most effective means available to achieve high quality results efficiently**



# Why Web-Based Reviews

- **Speed**
  - IT-enabled methodology enhancements to reduce reviewer and coordinator workload through automation
- **Storage and Updates**
  - Data from completed reviews occupies no physical space
  - Updates may be as simple as added new references
- **Facilitated Data Reuse**
  - Creating coded data from raw review data
  - Building sharable libraries of subject specific references



- **Commercial grade applications**
  - SRS (TrialStat, Canada)
  - EPPI-Reviewer (The Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) )
- **Home grown applications**
  - Typically Microsoft Access based
- **What about Review Manager?**
  - Analysis and reporting tool
    - Complimentary to web-based systematic review platforms
  - “Fat client” platform (requires software installation)
  - Single-user (uses check-in, check-out)



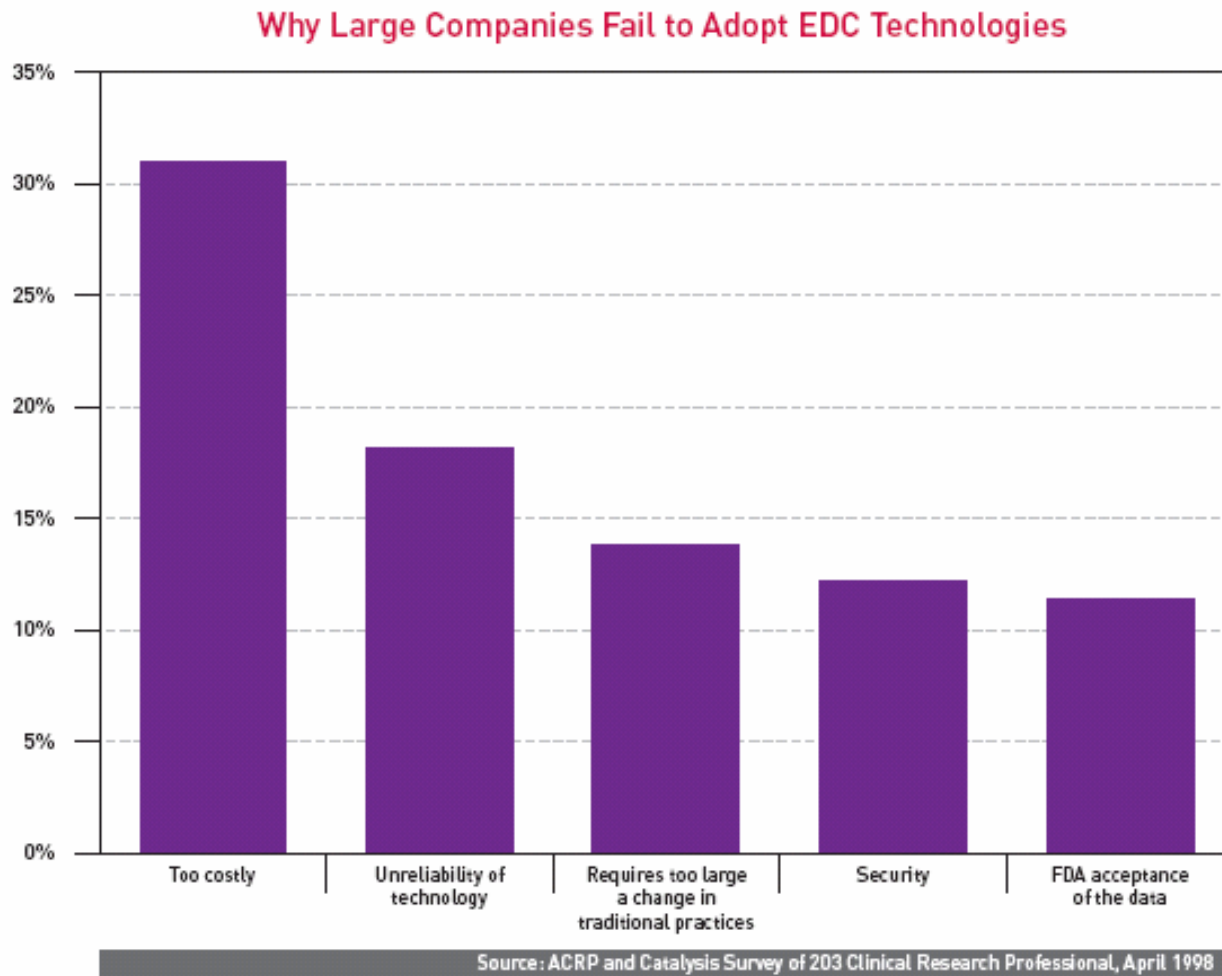
# Known Issues With Web-Base Reviews

- **System Reliability and Uptime**
  - Reliability is key to successful web-based reviews
- **Software Validation**
  - Rigorous software testing and validation or review results will be questionable
    - Question to ask: “Would my software, my development practices, and data my data management practices survive and FDA audit?”
  - Significant issue with home grown solutions
- **Security**
  - Access control and full audit trail required to ensure data integrity and confidentiality
- **Support**
  - Prerequisite for new and casual participants
- **Flexibility**
  - To be relevant to multiple groups, different protocols and methods should be supported



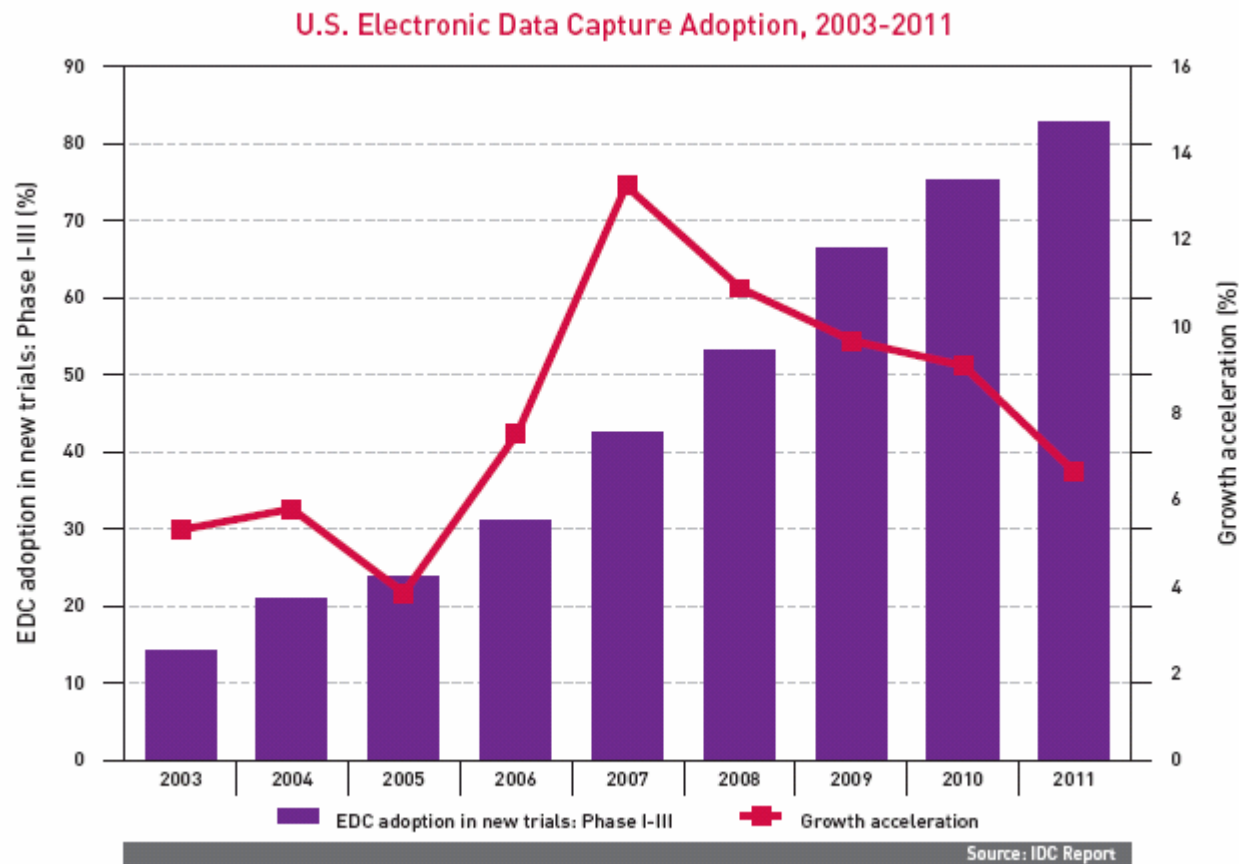
# Familiar Counter Arguments to Adoption

- Analogies With Clinical Trial Electronic Data Capture (EDC)



# Resistance is Futile

- Adoption of web-based SR technology has been slow growing but widespread adoption is inevitable (for good reasons)

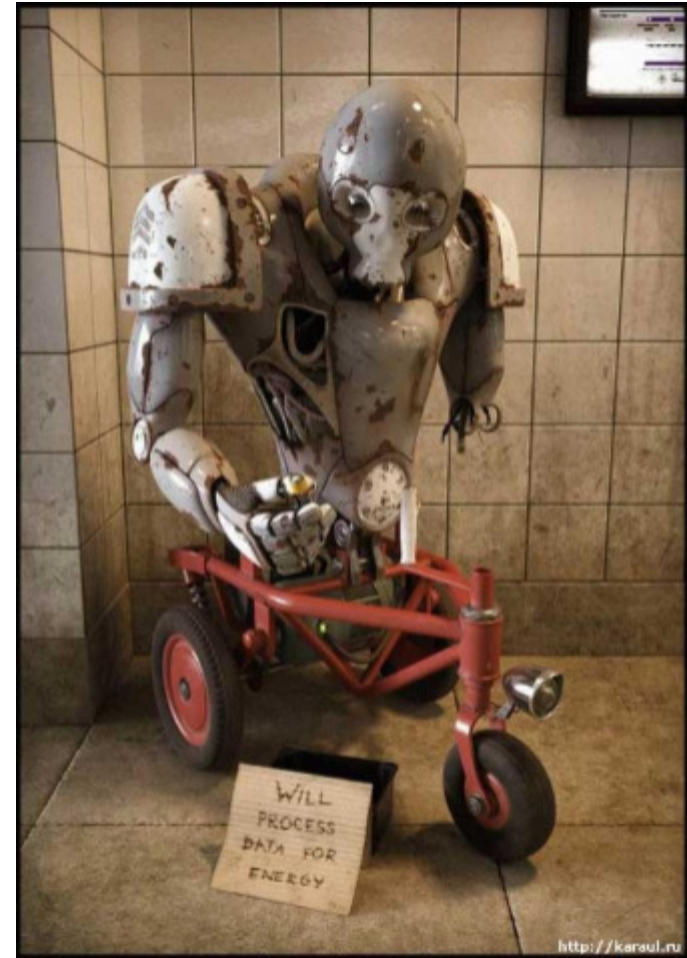


# Adoption Requires Commitment

- **Time and energy required to realize benefits**
  - The first attempt will be a learning experience
  - No direct mapping of paper methods to web-based methods
  - Technology learning curve
- **Coordinators must support the initiative**
  - Allow time for training and “redos”
- **Budgets/proposals must be recast**
  - Technology will offset traditional person hours, transportation, communication and office overhead



- **Camera-ready report authoring**
  - Version controlled
  - Word or PDF document generation
- **Improved data validation and cleaning tools**
- **Enhanced data-reuse and sharing mechanisms**
  - ESRNexus project
- **Automated Screening????**
  - EMISaR project - Stay tuned



*“The stone age didn’t end because they ran out of stones”*

- **Systematic reviews improve safety, cost and time needed to conduct of primary clinical research**
  - **Applicable to commercial and not-for-profit research**
- **Reviews are efficient and effective but offer significant operational challenges**
- **Web-based systematic reviews are in incremental improvement in alleviating some of the operational challenges to help deliver better results more efficiently**

