


integrated intelligence



**Comparative Effectiveness Analyses using
Simulated Treatment Comparison (STC)**

UBC
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Evidence Matters™

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**Context: Need for Methods for
Comparative Evidence**

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Disclosure: Employed by sanofi

My Talk Today

- **Environment : Comparative Effectiveness Research**
 - Requests from Health Authorities and HTA bodies
 - key to pharmaceutical companies/sanofi
 - a core element for drug development program in sanofi to support product relative value
- **Among multiples methodologies, why a Simulated Treatment Comparison?**

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Critical Questions to be Answered in a Changing Environment

- *What is the ADDED/RELATIVE therapeutic value?*
- *In which patient population?*
- *What are the longterm benefits and risks?*
- *Will efficacy translate into effectiveness?*
- *Transferability of data across countries?*
-

- Persisting economic constraints
- Availability of cheap generics with extensive evidence as standard of care in the majority of disease areas
- Increasing use of Health Technology Assessment: evidence and value based approaches to pricing & reimbursement
- Transition from individual payers to collaborating networks of payersand regulators (EuNetHTA)
- From data-monopoly of manufacturer to a distributed network of evidence bases (from trials and real world)

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Drug Development Being Mainly Focused on Regulatory Requirement Only, a Small Portion of the Questions are Answered

- It is widely acknowledged that the comparative effectiveness of most therapies is currently unknown (1)
- Commercially funded research has, understandably, been targeted at marketing authorization based on regulatory requirements that often allow for placebo-controlled or non-inferiority study designs (2)

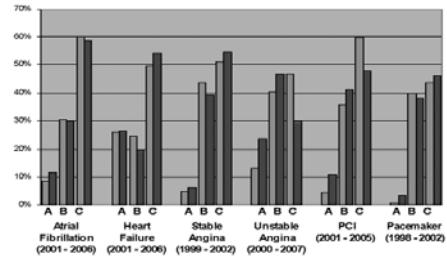
(1) Weinstein M, Skinner J. Comparative effectiveness and health care spending: implications for reform. *N Engl J Med* 2010;362(5):460-5.
 (2) Hochman M, McCormick D. Characteristics of published comparative effectiveness studies of medications. *JAMA* 2010;303(10):951-8.

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Much of Care Today is Not Based on Scientific Evidence

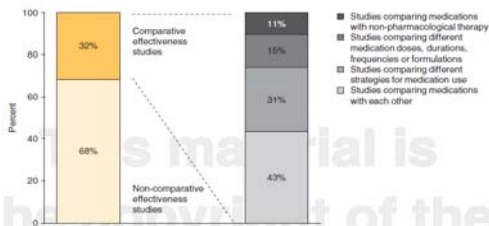
- Less than 20% of AHA/ACC heart disease management recommendations are based on a high level of evidence
- Over 40% are based on the lowest level of evidence
- Proportion of recommendations with high evidence levels has not increased over time



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Comparative Data would Ideally Come from Head-to-head Trials, but these are Rarely Available

- In a recent review 14% of studies were direct drug-drug comparisons



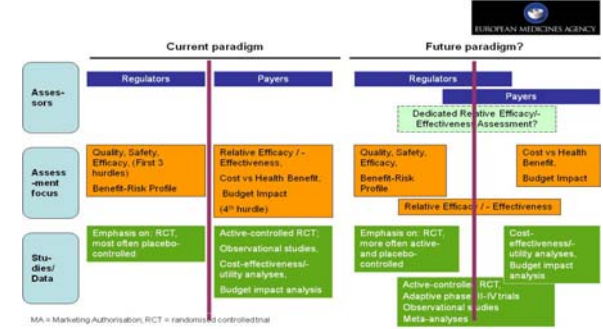
- A recent analysis of publications in the six medical journals with the highest impact factor considered all randomized trials, observational studies and meta-analyses published over a period of 16 months; a total of 1500 studies

Hochman M, McCormick D. Characteristics of published comparative effectiveness studies of medications. *JAMA* 2010;303(10):951-8.

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Emerging Interfaces Between Regulators and Payers in EU Around Relative Efficacy/Safety?



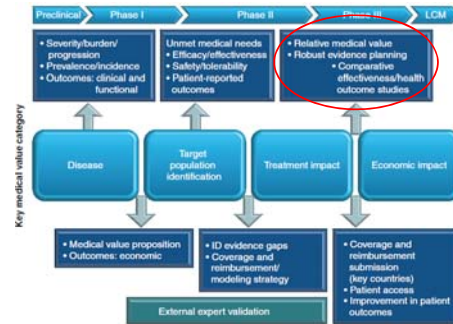
Eichler HG, Bloechl-Daum B, Abadie E, et al. Relative efficacy of drugs: an emerging issue between regulatory agencies and third-party payers. *Nature Drug Discovery* 2010;(9):277-91.

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Similar Approach in the US

- In February 2009, US president Barack Obama signed into law an act that allocates US \$1.1 billion for CER
 - This funding will be directed to the National Institutes of Health, the Department of Health and Human Services, and the Agency for Healthcare research and Quality
 - It is noted that the FDA is not mentioned in the act
- Establishment in the US of the Patient-Centered Outcomes Research Institute
 - Established by Congress through the 2010 Patient Protection and Affordable Care Act but is by law an independent, non-profit organization. PCORI is governed by a 21-member Board of Governors
- PCORI appears to be the institutional locus of CER in the future in the USA
 - Impact beyond the US: expanding the CER evidence base, CER resources and CER methods
 - CER findings will 'move market share' and call for higher evidence requirements and emphasis on head-to-head studies

Sanofi Entering a New Era of Drug Development



10 T Salimi, J-P Lehner, RS Epstein & SR Tunis. A framework for pharmaceutical value-based innovations. *J Compar Effect Res* (2012) (Suppl.1) :3-7.

All Direct Head to Head Comparisons Cannot be Performed...

- Transferability across countries/stakeholders will remain a challenge for drug development
- Choosing the most appropriate comparator
 - Regulator: Labeling / Recommended by guidelines
 - Payer: most used in real practice / cheapest in class / last in class -> will vary from country to country
- Endpoint on which judgment is based
 - Regulators: objective measures (e.g., HbA1C)
 - Payers : stronger emphasis on external validity / Health Related Quality of Life / workplace productivity

Mark Sculpher, Adrian Towse, Clifford Goodman and Bong-Min Yang. Comparative effectiveness for reimbursement: a comparison of international policies and methods. HTAI 2010 Maximising the Value of Health Technology Assessment, 6th – 9th June 2010, Dublin.

... There is a Need for Alternative Methodologies to Inform Decision

- Mixed Treatment Comparisons
 - Mixed Treatment Comparison is the standard when only aggregate information is available
 - It Provides an average effect across various trials/populations/follow-up time
- Real-world data analysis (claims, registries ..)
 - Informs about effectiveness of treatments/comparators in the real-life
 - Provides accurate estimation of safety
 - Informs about treatment patterns
- Simulation trials

Some Examples where Simulation could Bring Critical Information

- No data available on appropriate comparator for specific countries
 - Local practice recommends different treatments
 - Comparator used in real practice but not approved for the indication
 - Comparator recommended by Guidelines / compendium but not approved for the indication
- Hard endpoint as opposed to surrogate markers
Subgroup of patient where added therapeutic value is the highest
- Guidance for clinical trial designs
- ...

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...Availability of Data Source may Dictate Methodology

- Aggregate descriptive information and results of randomized clinical trials
- Real-Life data (claims databases, registries, ...)
- Randomized Controlled Trial (patient-level information)

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