

Effectiveness & Drug Test CoDevelopment

IOM Workshop, Washington DC, Feb 27, 2013

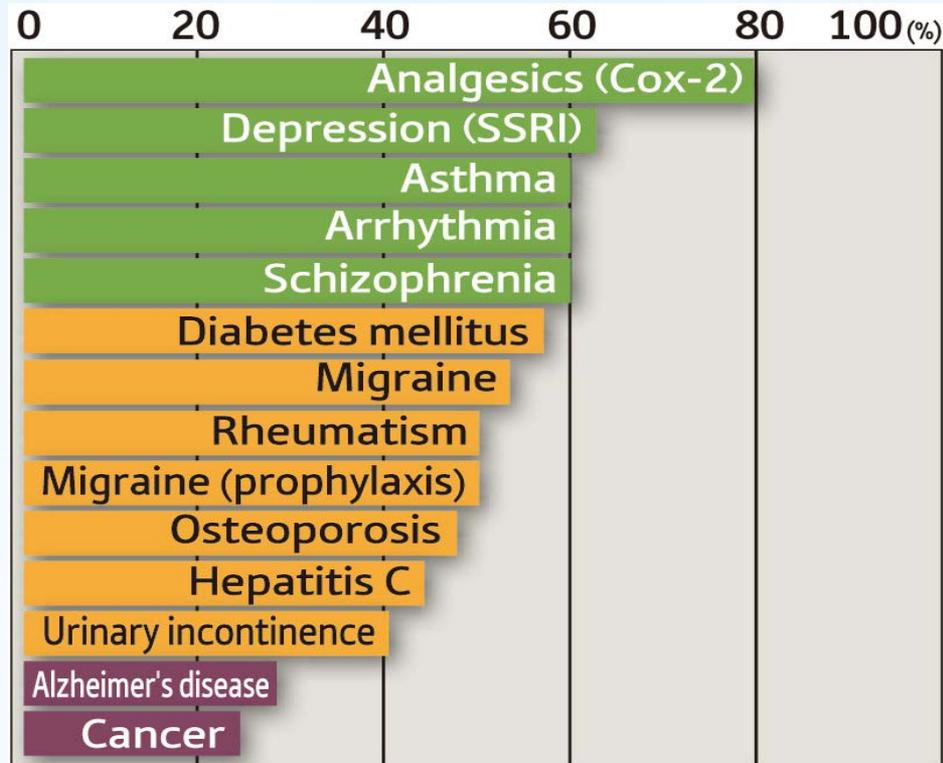
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- * Adequate to accomplish a specific purpose
- * Producing the intended or expected result
- * Actually in operation or in force, functioning

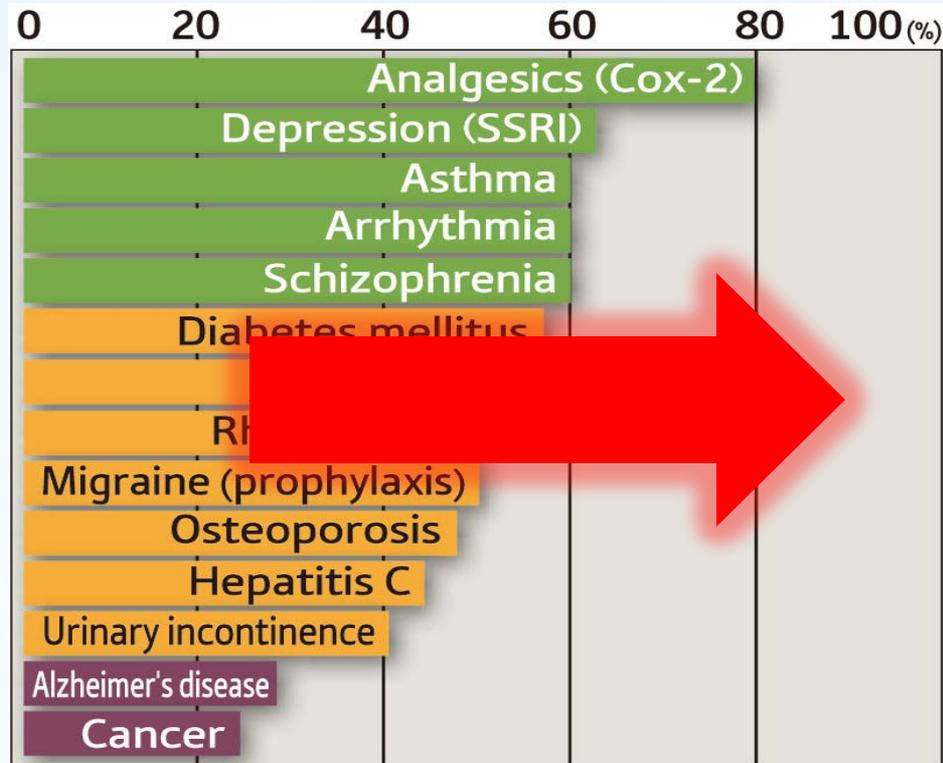
Effective(ness)

- * Power or capacity to produce a desired effect
- * Must be demonstrated to get drug approved
- * Usually demonstrated under ideal conditions (e.g. inclusion and exclusion criteria in clinical trial)

Efficacy



Real World Effectiveness of Drug Therapies



Point of Discussion

- * Precise characterization of disease opens opportunity to treat more effectively
- * Knowing a patient's (molecular) features may point to risks that can be eliminated
- * Based on measurement of patient's characteristics → requires a test

How?

- * Development of a test with a drug to make the use of the drug more effective and/or safer
- * A method to make medicine more precise

CoDevelopment: What it is

- * Approach to make trials smaller and cheaper
- * Paradigm to bring drugs to market faster
- * Discovery tool to identify subpopulations
 - * (A marker is known, and assumed to be relevant for a particular drug therapy. Hence the question is whether or not - and how - the simultaneous development, approval and reimbursement of both products is feasible.)

CoDevelopment: What it is *NOT*

- * Not because of FDA
 - * (If anything, FDA is helping: e.g. fast approvals of crizotinib, ivacaftor, telaprevir, etc.)
- * Drug development and test development are inherently different, difficult to coordinate
 - * Timelines do not align
 - * Resources are mismatched
 - * Market protection, IP significantly different

CoDevelopment: Why Is It Complicated?

*Aligning two very different business profiles

	Risk	Reward	Market
Drug	High	High	\$260 B*
Test	Medium - High	Low	\$5 B**

Challenge

**Kaiser data*

***UHC data for molecular diagnostics, not always associated with drug
all data US only*

- * Life Sciences (Biotechnology and Medical Devices) investing increased in terms of dollars but declined in deal volume for the third quarter of 2012 with \$1.7 billion going into 181 deals, comprising 26 percent of VC dollars invested. **Investment in Biotechnology increased by 64 percent in terms of dollars** and 22 percent in terms of deals with \$1.2 billion going into 116 companies in Q3. This increase is driven by a number of larger, follow-on rounds in the third quarter compared to Q2 when just \$755 million went into 95 companies. **Medical Device investing declined for the third consecutive quarter, falling 37 percent in dollars** and 27 percent in deal volume with \$434 million going into 65 companies, **experiencing the lowest dollar level of investment since 2004**. Overall, Life Sciences investment for the first three quarters of 2012 is down 19 percent in dollars and 12 percent in deals from the same time period in 2011. *

VC Investments in Life Science

- * Assume intended to treat population = 1M
- * Test costs \$500
- * Population reached: 20% = 200,000
- * Potential market size = 200,000 x \$500 = \$100M

- * Initial investment: \$100M
- * Profit margin: 50%
- * 2 years after launch, investment recovered

The Market Size Issue (Investor View)

- * Assume 4 years of development
- * Test starting to make profit after (4+2) 6 years
- * Assume desired (and modest) 3x ROI = \$300M
- * \$50M profit/year (50%) → $\$300\text{M}/\$50\text{M} = 6$ years
- * 12 years until desired ROI
- * Corresponds to 9.5% annual growth of capital

The Market Size Issue (Investor View), cont'd

But,...

...this does not include, for example:

- Development failures
- Price deterioration of diagnostics
- Competition (e.g. for same marker)
- Newer, better markers

* (So why would anyone invest in this market, anyway?)

The Market Size Issue (Investor View), cont'd

- * New drugs priced are record levels (e.g. crizotinib, ~\$10,000 per patient per month)
- * EML4-ALK test reimbursed at \$128.48*
 - * Required for crizotinib
- * Decreases in new reimbursement rates for 2013 (e.g. BRAF -78%, EGFR - 62%)

Increasingly Disparate Reimbursement Rates

- * Rewards (and stakes) for drug development higher than rewards for test development
 - * Not a relationship between equal partners
- * Goals of drug development usually control decisions in codevelopment effort
 - * They don't have to be necessarily different from goals of test development
 - * But also doesn't mean that they are aligned or even understood by respective partners

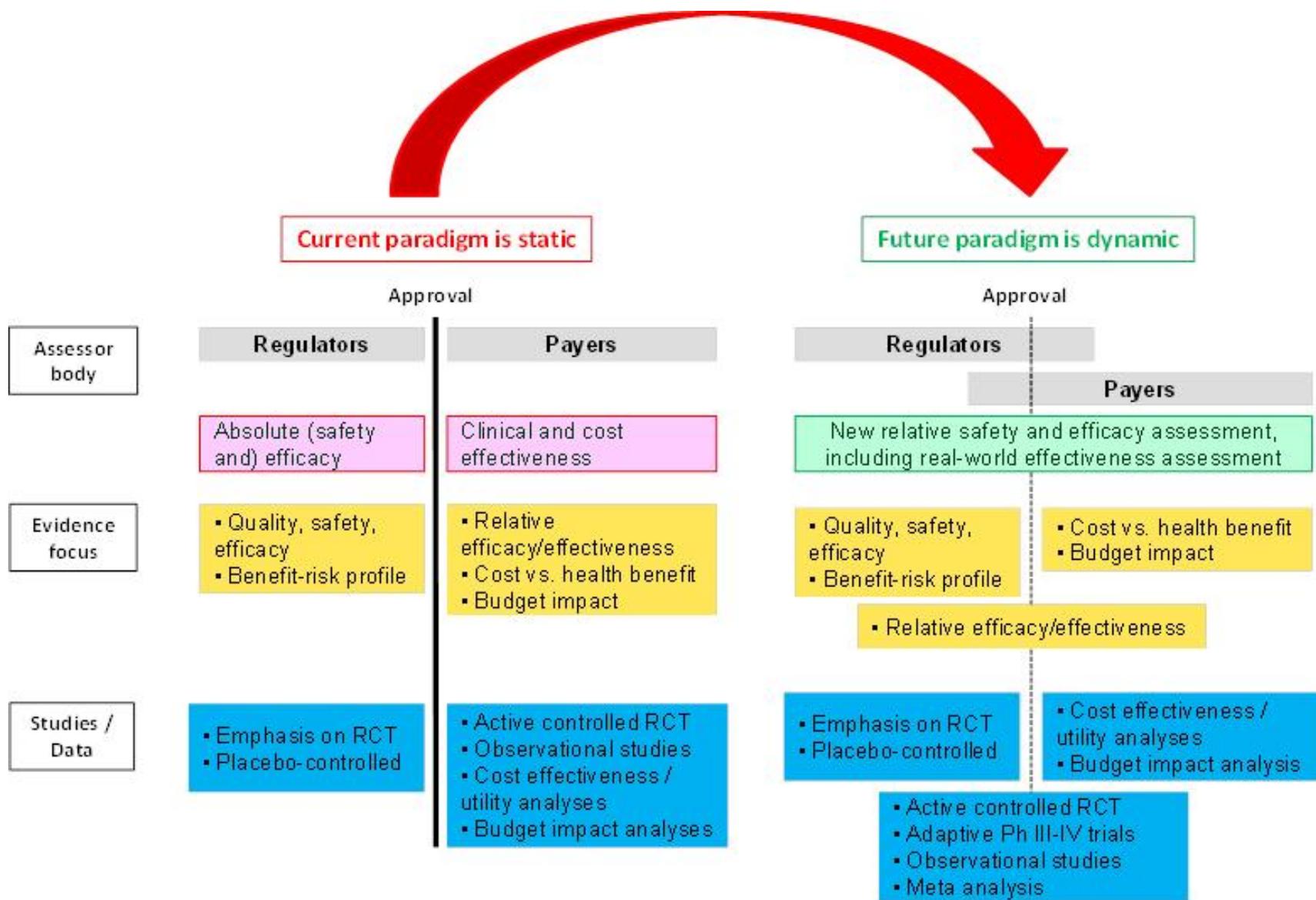
The Reality Is...

- * Assume effectiveness requires (drug and) test
 - * Test adds to effectiveness of therapy
 - * Compare effectiveness with and without test
 - * Calculate increase in effectiveness
 - * Calculate value of test
- * **Pay for outcome, value-based ($R_x + D_x$) pricing**
- * **(If personalized medicine works, this should be easy - and if it doesn't, we don't need it)**

Possible Solution:
Focus on Outcome/Value

- * We don't usually pay for products that don't work - why should health care be different?
- * Codevelopment is aligned with payers' demand for more evidence of outcome; also viewed as opportunity to reduce cost
 - * Oddly however, the same payers also exercising pressure on pricing for tests - makes no sense!
- * Accelerate regulatory approval and reimbursement decisions through convergence of efficacy and effectiveness data generation

CoDevelopment: Paying for Effectiveness



- * Selection of clinical endpoints: must be relevant for real world clinical decision making
- * FDA and payers should require “CoPresence” of drug and test manufacturers at all meetings relevant for codeveloped products
- * Test must pass regular proficiency testing, market performance of codeveloped product should be monitored

New (Team) Processes for CoDevelopment

- * Exclusivity for test may not be guaranteed
 - * Other manufacturers or labs can develop new test
 - * Not necessarily bad: supports innovation of better tests
- * Two models to incentivize test manufacturing during drug development
 - * Early test development fully compensated for by pharma
 - * Percentage of drug revenue from sales based on decisions made using test

Alternative Risk Sharing

Summary

- * Effectiveness does not equal efficacy
- * Effectiveness is what matters in real world
- * Market for tests usually undervalued
- * Alignment of drug and test development is challenging
- * Changing focus from cost of goods to value is needed
- * Merging regulatory and reimbursement strategies is possible, new processes may be required
- * Alternative risk sharing models can be explored

Thank You

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