

The Economic Challenges Of Integrating Pharmacogenomics Into Clinical Practice

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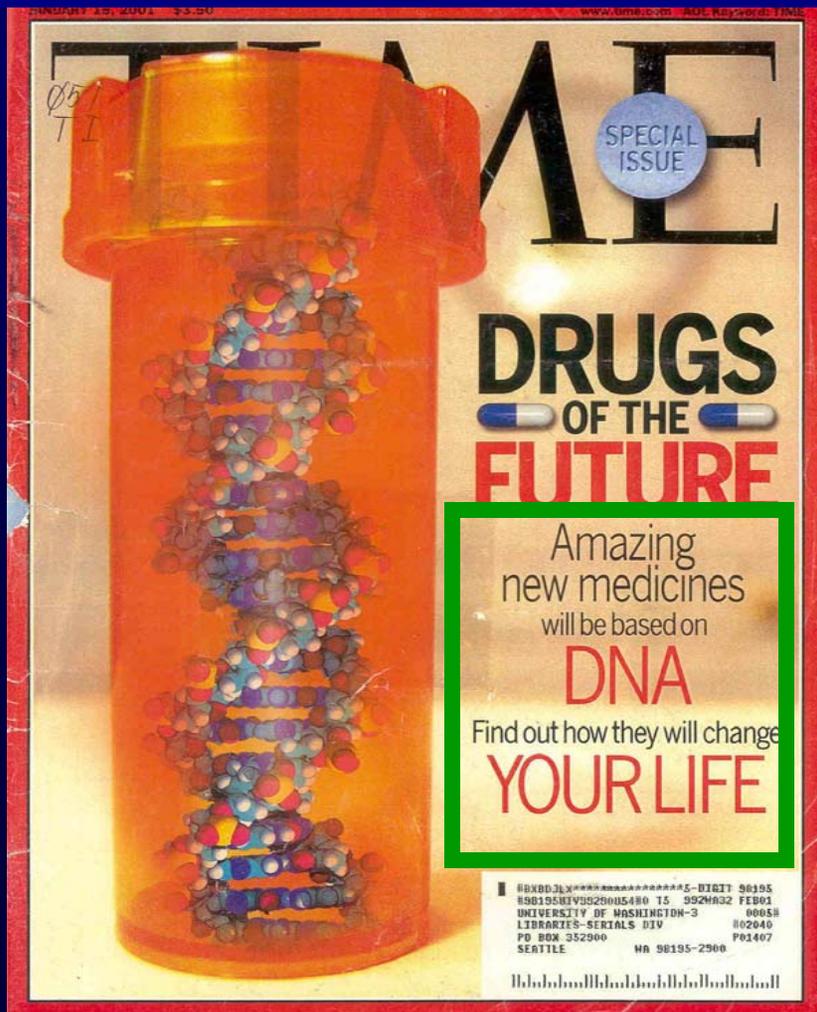
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“Hype” that pharmacogenomics (PGx) would revolutionize medicine

- Time magazine cover 5 years ago....



Where is PGx Now?



Get on the Bus or Get Run Over?

OR



Where's the Beef?



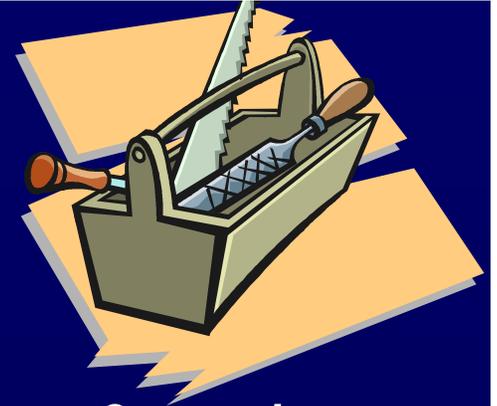
Economics can
help figure it out

Objectives

To discuss economic challenges of integrating PGx into clinical practice

1. Discuss steps needed to *maximize value* of PGx & how an economic perspective can be helpful
2. Use illustrative case studies
 - Herceptin
 - Iressa
 - CYP450 testing (e.g., AmpliChip)

Why is Economics Relevant?



Provides toolbox & tools

Economics focuses on:

- *Incentives*
 - Why PGx does/does not get adopted
 - What type of incentives will *maximize value* of PGx
- *Value*
 - What is “value” of PGx
 - How is value defined?
 - How does value change by perspective?
 - How can value be measured?

What is an Economist Doing in a Nice Place Like This?



My Perspective: Wearing Three Hats

1. Academic

- Research on application of economics to PGx
- Research on drug safety & policy issues

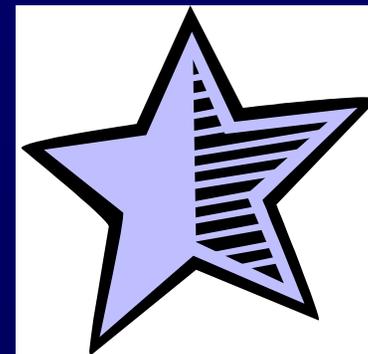
2. Government

- Advisor to the FDA on PGx
- Member of CDC-sponsored national group on application of genetic testing (EGAPP)

3. Industry

- Previously consultant to biotechnology companies on how to measure value

Three Steps to Maximize Value of PGx



1. Understand importance of economic & non-economic incentives
2. Consider value from multiple perspectives
3. Use innovative approaches to address new paradigms

Illustrative Case Studies

- Trastuzumab (Herceptin®, Genentech)
 - Treats HER2/neu+ breast cancers
- Gefitinib (Iressa®, AstraZeneca)
 - Treats non-small cell lung cancer
- Testing for CYP450 drug metabolizing enzymes
 - One test approved by FDA: AmpliChip® CYP450 test (Roche Diagnostics)
 - o Tests for two key drug metabolizing enzymes (CYP2D6, CYP2C19)

(1) Understand Importance of Economic & Non-Economic Incentives

- PGx adoption will only occur if properly structured, aligned, & built-in incentives
 - E.g., Often noted that physicians need to be “trained” about genetics
 - Won’t do the trick unless there are incentives!!
- *But* incentives push in different directions
- *But* incentives for adoption vary based on characteristics of PGx intervention

PGx Characteristics Providing Incentives FOR Adoption

- If life-threatening vs. chronic condition
- If strong advocacy group or industry interest
- If high reimbursement coverage & rates
- If PGx used during drug discovery/development vs. later
- If PGx used for immediate vs. future tx decision
- If PGx used for focused, narrow tx decision
- If PGx can be used for off-label indications
- If PGx used for ongoing monitoring vs. one-time
- If targets acquired v. inherited mutation
- When PGx test *dictates* what tx will be used vs. *suggests* tx or dosage

PGx Characteristics Providing Incentives for Adoption (cont.)

- PGx more likely to be implemented if PGx NOT considered “PGx” (!)
 - But instead considered “personalized medicine”, “targeted therapy”, or “smart drugs”
 - Why?
 - Builds on existing approaches (e.g., use of family history)
 - Easier to understand & support concept of “personalized medicine” vs. “genetic testing”
 - Emphasis on drug vs. person

Case Studies: Herceptin

Illustrates fast & successful adoption

- Herceptin best-known example of personalized medicine
 - Although often not considered “pharmacogenomics” since testing is of tumor
- Proved that targeting to small populations CAN be feasible and profitable
 - Sales keep increasing (\$479M in 2004, 70% increase in 3rd quarter)
- Important to note that testing is for GATEKEEPING, not for dosage decisions

Case Studies: Iressa

Illustrates fast but (currently) unsuccessful adoption

- FDA accelerated approval
 - But drug now essentially withdrawn from market
 - Post-approval clinical trials showed no significant survival benefit
- Appears to benefit specific populations
 - But until recently no diagnostic has been available so drug could not be targeted
 - Test now developed but limited availability, expensive (\$975), & unknown benefits

Case Studies: CYP450 Testing

Illustrates slow adoption

- Many implementation challenges including:
 - Multi-factorial nature of drug response
 - Lack of data linking mutations & clinical outcomes
 - Variability across & w/in drug classes
- Testing is of PERSON
 - Thus raises more ethical issues
- Testing not a strict “gatekeeper” test
 - Thus incremental benefit harder to measure

(2) Consider Value from Multiple Perspectives

- All stakeholders want evidence of VALUE
 - But perspectives differ by stakeholder
- From societal perspective, little documentation yet of value of PGx
 - Few economic analyses to date
 - Our systematic review found only 11 cost-effectiveness analyses of PGx interventions (Pharmacogenomics, 2004)
 - Limited range of conditions studied
 - Mixed results as to whether cost-effective

Challenges to Determining Value of PGx

Differences in Perspective

- Value determinations are often made *before* product reaches the clinical setting
 - Determinations along entire pipeline prior to adoption: discovery, development, regulation, & reimbursement

Thus:

- Economic incentives need to be considered AND
- Economic evaluations need to be conducted

....*Before* PGx intervention is adopted if societal benefit is to be maximized

Challenges to Determining Value of PGx

Technical Issues

- Lack of data
 - Linking PGx to outcomes
 - Comparative effectiveness of therapeutics
 - On products themselves (proprietary)
- Need to evaluate complex multi-factorial conditions
 - Diagnostic/drug combinations more complex to analyze than separate interventions

Challenges to Determining Value of PGx

Policy & Political Issues

- Few incentives to assess economic value from *societal* perspective
 - Advocates, industry, FDA, CMS, insurers do not usually evaluate PGx from economic, societal perspective
- PGx often has benefit of PREVENTING what has not occurred
 - Value of prevention harder to measure
 - E.g., avoiding adverse events
- Value of diagnostics often harder to measure
 - Up-front PGx testing cost perceived as higher than downstream savings

Case Studies: Herceptin

Illustrates successful adoption despite lack of documentation of societal benefit

- Herceptin is expensive ~ \$3000/month
- Increases median survival by few months
- Cost-effectiveness analyses are inconclusive
 - Elkin (2004): \$125,000 per quality-adjusted life year gained (>\$50K threshold commonly used)
- Outside of US, approval of drug for national formularies was slow because of concerns about cost-effectiveness

Case Studies: Iressa

Illustrates that failed adoption has potential to create large societal losses

- Withdrawal of drug from market incurs large losses not only to company but also society
 - Patients do not benefit
 - Expense of regulatory efforts
 - Increases concerns about drug safety

Case Studies: CYP450 Testing

Illustrates where widespread testing could have huge economic & health impact

- But requires creative and complex approaches to assessing value
 - Initial step was our study that found potential linkage between adverse drug reactions and P450 mutations (JAMA, 2001)

Case Studies: CYP450 Testing

- More recent study found CYP2D6 testing COULD have large impact because many drugs metabolized by CYP2D6 (Nat Rev Drug Discov, 2005)
 - Relevant to 189M prescriptions and \$12.8B expenditures/annually in US
 - Particularly mental health and heart disease drugs
- BUT insufficient data to assess impact of CYP2D6 testing
 - Very limited data on clinical outcomes of testing
 - E.g., only one package insert (Strattera) mentions availability of CYP2D6 testing

(3) Use Innovative Approaches to Address New Paradigms

- Diagnostics & co-developed diagnostics/drugs will play *increasingly* important role
 - Requires integration of historically divided industries and regulatory mechanisms
 - Requires early consideration of diagnostics
- Three key barriers in diagnostic pipeline (results from ongoing FDA study)
 1. Money (investment & reimbursement)
 2. Availability of data & samples
 3. Clinical utility of tests often not evaluated & thus difficult to demonstrate value of diagnostics

Case Studies: Herceptin & Iressa

Illustrates that will be challenging to develop & determine most appropriate diagnostic

- Several tests approved for use with Herceptin
 - But much debate over which test is most appropriate
- Development of diagnostics often requires multiple stakeholders merge forces
 - Academia, Industry, FDA

Case Studies: CYP450 Testing

Illustrates that will be challenging to adopt PGx when relevant to multiple diseases & drugs

- P450 testing is done once/lifetime
- Results are relevant to multiple diseases, drugs, & clinical specialties
 - So who will advocate for testing?
- Is test for diagnosis or screening?
 - Important because, e.g., Medicare covers “diagnostic” but not “screening” tests – but which is it?

Case Studies: CYP450 Testing

- Unclear whether:
 - Consumers will seek out?
 - Providers will provide?
 - Industry will have incentives to develop tests?
 - Insurers will cover “screening” tests?

Summary: Next Steps to Address Economic Challenges of Integrating PGx into Clinical Practice

1. Understand importance of economic & non-economic incentives

- Incentives matter!
- Incentives are often contradictory
- Incentives can be shaped by health policies

2. Consider value from multiple perspectives

- Definitions of value will vary across stakeholders
- But value must be determined
 - If not done from societal perspective then will be driven by other perspectives
 - Need incentives for economic research

Summary (cont.)

3. Use innovative approaches to address new paradigms

Requires truly *multi*-disciplinary approach & innovative funding mechanisms

- But social science lags behind basic science
- Why? Risky, requires more in-depth understanding of basic & clinical science, hard to get funding

Requires development of evidence base

1. Pharmacogenomics Research Network
 - Although application issues not included
2. Evaluation of Genomic Applications in Practice and Prevention (EGAPP)
 - Although will need to be institutionalized in order to continue

Conclusions

- PGx is here now & will keep coming!
 - *Inevitable* push towards PGx because part of larger trend towards “personalized medicine”
 - Genetic information is ONLY one piece but CRITICAL piece
- Government has critical role in facilitating appropriate use of PGx in order to maximize its benefit
 - In shaping incentives
 - In ensuring that value gets measured from a societal perspective
 - In facilitating innovative approaches

Thank you