Forces Shaping Technology Diffusion: How Applicable to Genomic Innovations?

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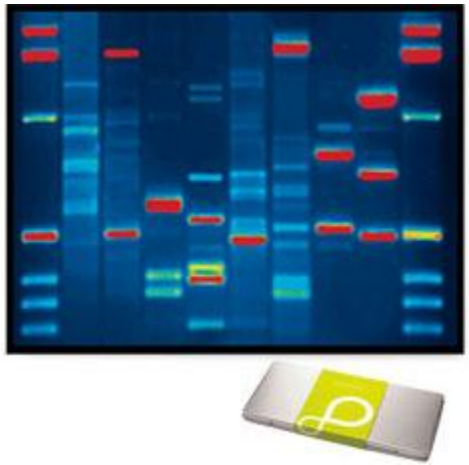
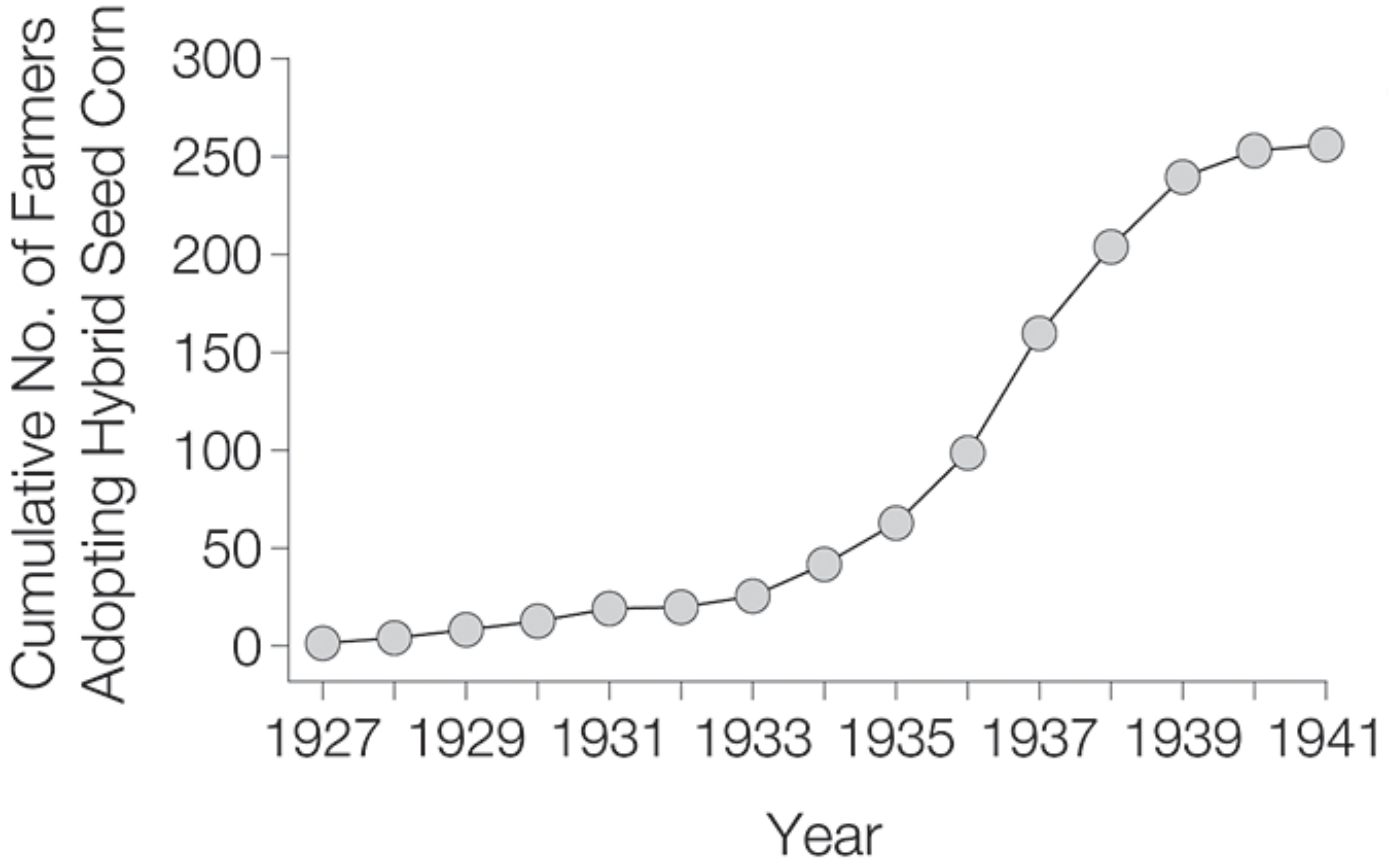
Genomic Medicine

- Improved understanding of genetic & molecular basis of disease
- Increasingly leading to development of interventions -- genetic testing, gene-based therapy, pharmacogenomics
- Permeating other areas of life, even art
- Spotlight on diffusion: How best manage challenges in adoption and use?



Modelling Diffusion



Griliches, Z. Econometrica 1957

Determinants of Rate of Diffusion

- Characteristics of the technology (available alternatives, marginal benefits, severity & prevalence of illness, costs, complexity)
- Regulatory agencies and payers as gatekeepers
- Characteristics of potential adopters (physicians, hospital adm., trustees etc)
- Economic incentives
- Socio-cultural (ethical) factors

Critical & Under-examined Forces in Medical Diffusion

- Diffusion literature: technology seen as 'static'; innovation continues in clinical practice
  - Adoption decisions face uncertainty about ultimate value of a technology
- Stakeholders seek evidence to guide adoption decisions
- Bring distinct readings to decisions with great implications for quality, cost, fairness
  - Preferences and values of stakeholders

Actual Use in Clinical Practice

Locus of ‘Down-stream’
Learning and Innovation

Refinement of Patient Selection Criteria

- Expansion of target population -- CABG
  - Only 4% of CABG patients today would have met eligibility criteria of initial trials
  - Use expanded to patients with acute MI, women, elderly, etc. – all excluded in initial trials
- Reduction of target population – Ca Ch Blockers
  - Sub-groups of CVD patients (such as post-MI and CHF)

New Indications of Use

DRUG	ORIGINAL INDICATIONS	NEW INDICATIONS
beta-blockers	angina pectoris, arrhythmias	hypertension, anxiety, CHF, etc
aspirin	pain	stroke; CAD
anticonvulsants	seizure disorders	mood stabilization
alpha blockers	hypertension	prostate disease
fluoxetine (prozac)	depression	bulimia, OCD
thalidomide	anti-emetic & tranquilizer	leprosy; graft-vs-host

Integrating a Technology into the overall Management of Patients

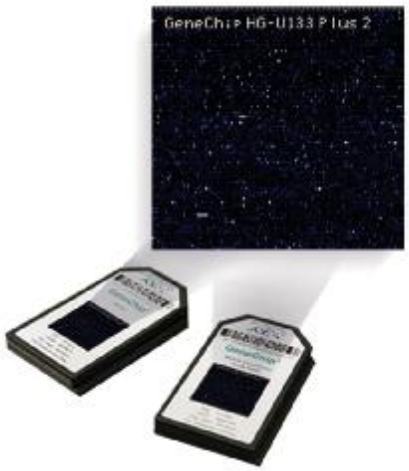
- LVADs CMS approved for ESHF in 2003
- Changes in operative technique
- New ways to prevent infections
- Changes in anticoagulation regimens
- Reduction in AE profile & hospital LOS
  - Rematch LOS : 44 days
  - Post-Rematch LOS : 33 days

Diagnostic Technologies that Outpace Prognostic or Therapeutic Knowledge

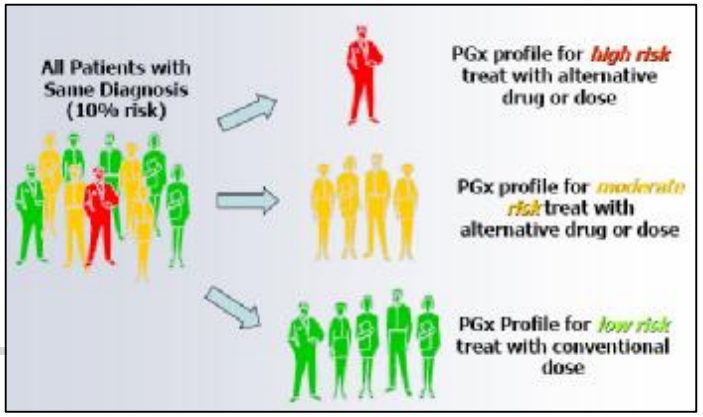
- Can identify abnormalities but uncertainty lingers about prognostic implications and need for treatment
  - Mammography/DCIS, PSA testing, MRI & unbled brain aneurysms
- Results in
  - Significant variation in rates of further testing and treatment patterns
  - Many of which may not be necessary

Diagnostic Technologies that Enhance Prognostic Abilities

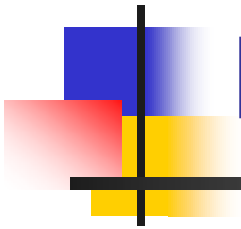
- Breast cancer
  - Many women receive adjuvant chemo
  - New gene chips specify prob. recurrence
  - Target need for chemo Rx in addition to radiation
- However, these tests –uncertainties
  - Positive test not always indicate development of disease
  - Due to incomplete penetrance, variable expressivity, other genes, & environmental factors



General Theme



- New technologies relatively 'primitive' when introduced, slow diffusion
- Use produces downstream learning, may lead to technology modifications or refinements of application
- These refinements include
  - Prognostic understanding deepens about genes-environmental factor interactions in disease (Burke, 2007)
  - Integration with appropriate surveillance & Rx regimes, for spectrum of at-risk patients (Burke, 2004)
- Clinical utility of tests, confirmation in large well-defined populations & pragmatic clinical trials



Evidence as Critical Factor

The FDA and Diagnostic Tests

- Key in shaping ev/adoption & FDA active role
- Traditional: FDA (kits) & CMS (laboratory)
- Amplichip CYP450 (2004) higher level of review
- Value of diagnostic tests harder to measure
- Evidence directed at accuracy
- Insights about clinical utility often emerge in post-marking setting

Uncertainty About New Test Interpretation

- AlloMap® gene chip (2005) – detects acute cellular rejection in heart Tx
- Comparison to biopsies, â positive predictive value, but non-invasive
- Uncertainty about clinical utility, many centers use test as add-on not substitution
- Cardiologist comfort with interpreting genomic testing varies

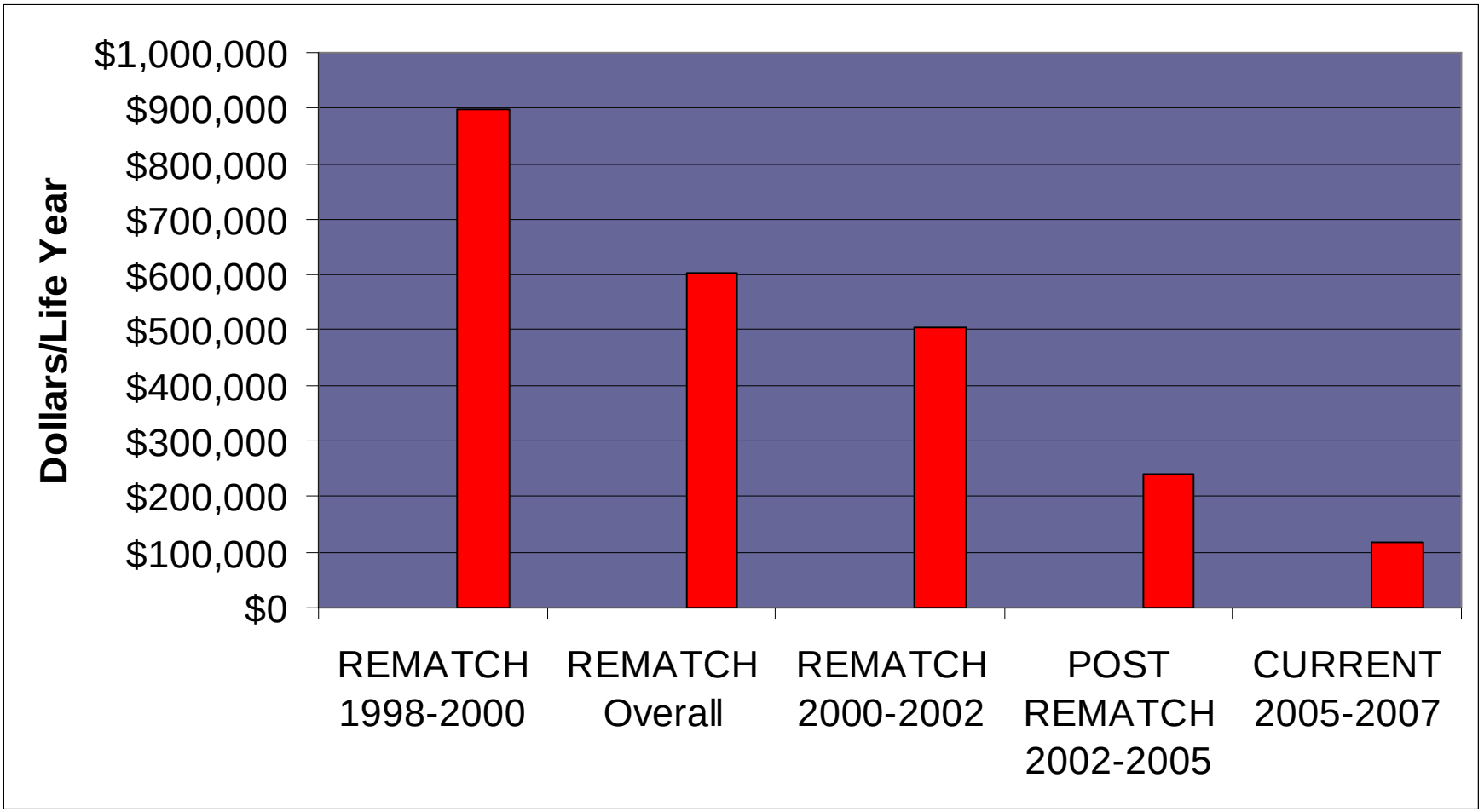
FDA and Pharmacogenetics

- Integration of diagnostics and drugs will require bringing together of regulatory pathways
- Successful example: HER2 testing and Herceptin
- Fast-track process, FDA joint approval (1998) with coordinated labeling
- Clear relationship biomarker and drug response, clear survival benefit for life-threatening condition (Phillips, Health Affairs, 2006)
- Tests that involve more ambiguity about their ultimate value, rigorously conducted pre- and post-marketing studies will be key

Coverage & Reimbursement

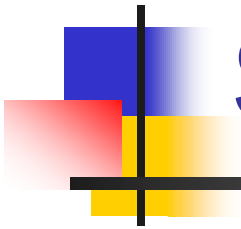
- Payers struggle with trade-offs between costs and benefits
- Although not coverage criterion for CMS, other payers have incorporated it into their decision-making
- CEA of emerging, novel technology is challenging
- Substantial post-marketing innovation, and strict adherence to a CE threshold (eg $100K), may eliminate important technology before had a chance to reach full potential

Changing CE Ratio of LVADs



Applicability to Genomics?

- Post-marketing innovation & learning by using will be feature of genomic interventions
- CEAs need to incorporate such learning into sensitivity analyses in a systematic manner
- Decision-making needs to accommodate some flexibility to allow for short-term inefficiencies to garner long-term value
- Optimal learning takes time and experience, payers may be uncomfortable in underwriting alone
- Public-private partnerships?



Socio-Cultural Factors

Preferences and Values of Stakeholders

Adoption of Genetic Tests

- Even if covered, patients may decide to pay-out-of pocket -- confidentiality
- Concerns about employer and insurance discrimination
- Raises concerns about equity; e.g. obstacles to access for those who don't have the means to pay

Knowledge of ‘Unmodifiable’ or Uncertain Health Risks

- Tests that identify predisposition & susceptibility to future diseases, if no cures or only Rx with limited effectiveness
- The Huntington’s Chorea testing dilemma
- Affected by patient preferences and perceptions of value of health risk information

Diffusion is Important Process

- By which health, social & economic rewards of invention are reaped
- More than that – intrinsic part of innovation process
- Diffusion is learning process, & fundamental aspect of learning is reduction of uncertainty
- Downstream learning can lead to Δ in tech
- pose new questions for basic/translational research, and enrich their ultimate payoff

Concluding Observations

- Diffusion hinges not only on the benefits provided by new interventions
- But also on institutional environment in which they are to be embedded
  - Pts/consumers/physicians what to do with new sort of risk information
  - FDA how to deal with genetic diagnostic tests & diagnostic/drug combinations (PGx)
  - Insurance conduct and interpretation of CEA of emerging technologies
  - Policy world -- insurance/employers deal with privacy/discrimination issues