Comparative Effectiveness and Cost-Effectiveness Analyses Frequently Agree on Value

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(Glick HA, McElligott S, Pauly MV, Willke RJ, et al. Health Affairs. 2015; 34: 805-11.)

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Opinions are mine alone

US Health Care Spending Crisis?

- Common to assert that continual increase in US health care spending can be stopped by:
  - Adopting and using electronic medical records
  - Increasing funding for prevention
  - Performing comparative effectiveness analysis and adopting the most effective therapy

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HENRY'S **OPINION**

- Big lies in health care:
  - Using electronic medical records saves health care $
    - Little to no evidence that it's true
  - Increasing funding for prevention saves health care $
    - Most studies conclude that prevention increases rather than decreases health care costs
      - E.g., Russell LB. Preventing chronic disease: an important investment, but don't count on cost savings. Health Aff (Millwood). 2009;28:42-5.
    - Then argue prevention valuable whether or not savings accrue
  - Current talk doesn't address either claim

HENRY'S **OPINION** (2)

- Big lie #3
  - Performing comparative effectiveness analysis and adopting the most effective therapy saves health care $
  - Topic of today's talk
- Henry's view: Only way to effectively control health care spending:
  - Given health needs, available Rx, and health care budget, identify what we are willing to pay for health (in U.S., 100k/QALY? / 3.6M baht)
  - Determine – using scientific procedures – that some therapies provide too little health care value
  - Do not use public funds or require private insurance to provide these therapies

Motivation for Current Study

- Comparative effectiveness research (CER) seeks to assess interventions' incremental clinical benefit
  - Advocates sometimes suggest that adoption of most effective therapy reduces HEALTH CARE COSTS
  - But decision making based on CER alone may lead to adoption of expensive interventions with only small incremental clinical benefits
- Cost-effectiveness analysis seeks to assess interventions' incremental value/net benefit
  - Advocates sometimes suggest that rejection of low value therapies increases likelihood of controlling health care costs
- In US, explicit use of cost information and formal CEA for decision making currently contentious

Concerns With Cost-Effectiveness Analysis

- Technical:
  - e.g., do empirically derived QALYs correctly quantify trade-offs in length of life, quality of life, and cost
- General:
  - Public distaste for notions of rationing of health care
  - Fact that rejection of new therapies may inhibit innovation / new improved therapies
  - Unease about having clinical decision making scrutinized based on costs
- In response, enabling legislation for the Patient-Centered Outcomes Research Institute (PCORI) states that it "shall not develop or employ a dollars-per-quality-adjusted life year…as a threshold to establish what type of health care is cost-effective or recommended"

Current US Users of CE and CB Analysis

- Common belief: CE/CB not used in US
  - True that a large number of agencies are barred from using
- But…
  - NIH expert guideline panels and Environmental Protection Agency can and do use
  - Chambers et al.: By law, can't be used by Medicare, but lack of estimate of cost-effectiveness associated with decreased likelihood of Medicare coverage decisions
  - Medicaid, Vaccines for children (But not formally)

Current Users of CE and CB Analysis (2)

- U.S. cont.
  - Aspinall et al.: Veterans Health Administration "has emphasized use of cost-effectiveness data, especially for newer, costly drugs"
  - Neuman and Bliss: 12% of FDA drug advertising (DDMAC) warning letters between 2002 and 2011 cite health economic violations
  - Academy of Managed Care Pharmacy guidelines for pharmacoeconomic submissions to formularies (yet)

Study Aims

- To address public/political cost-effectiveness "fatigue":
  - Quantify frequency of agreement between results of CER and CEA
  - Identify possible systematic characteristics of interventions that we can identify *a priori* that predict agreement between CER decision making and CEA decision making
- Secondary objective (requested by reviewers and journal editors):
  - Quantify savings that might accrue if we rejected therapies with incremental cost-effectiveness ratios above some "social value of a QALY" thresholds
    - Typically referred to as "willingness to pay"

Methods

Study Sample

- Study sample drawn from Tufts University Center for the Evaluation of Risk in Health CEA Registry
  - Comprehensive database of peer-reviewed articles

Exclusion Criterion	N
Initial sample	6793
Non-US studies	3718
Studies prior to 1990	87
Missing QALYs	961

TOTAL: 2027 ratios from 819 articles

Agreement

- Primary outcome: Binary variable representing agreement (coded as a 1) and disagreement (coded as a 0) between adoption recommendations from CER and CEA

Comparative Effectiveness Recommendation

- Adopt therapy with larger point estimate for effectiveness
  - Do not require statistical significance
- In most formal comparative effectiveness research, effectiveness measures will be disease-specific clinical outcomes or mortality
  - e.g., changes in HbA1c, mm/Hg of blood pressure, or mmol/l of cholesterol
- In current study, effectiveness measure is QALYs derived from denominator of cost/QALY ratio
  - e.g., if surgical treatment adds more QALYs than medical treatment, we consider surgical treatment to be recommended

Cost-Effectiveness Analysis

- Cost-effectiveness analysis: Compares difference in cost with difference in effect between pairs of therapies

$$ICER = (C_1 - C_0) / (E_1 - E_0)$$

- Ratio generally interpreted as extra payment per extra unit of effectiveness for more effective therapy
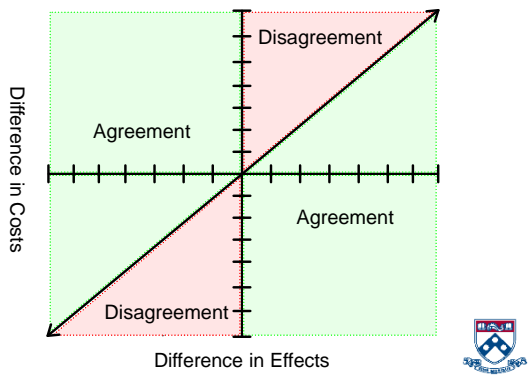
Cost-Effectiveness Recommendation

- Adopt therapy with larger point estimate for QALYs if it:
  - Costs less and does more than the alternative or
  - Has a cost-effectiveness ratio less than or equal to willingness to pay per QALY
    - i.e., if, compared to medical treatment, surgical treatment adds more QALYs, costs more, and has a cost per QALY ratio less than willingness to pay
      - e.g., $\leq$ $US 100,000 per QALY
- Adopt therapy with smaller point estimate for QALYs if therapy adds more QALYs, costs more, but has a cost per QALY ratio greater than willingness to pay
  - e.g. greater than $100,000 per QALY

  Latter finding indicates disagreement

Don't Distinguish Between "Types" of Agreement

Difference in Costs (y-axis)
Difference in Effects (x-axis)

- Disagreement (top right region)
- Agreement (top left region)
- Agreement (bottom right region)
- Disagreement (bottom left region)

"Social Value of a QALY Threshold"

- Some countries have generally recognized ranges of value
  - In UK, <20k GBP considered good value
  - 20k-30k, may be considered good value
  - >30k, needs special circumstances to be considered good value
- In US, little agreement about willingness to pay per QALY
  - Potentially ranges between (2010) USD 0 and 200k
  - Primary analysis of predictors of agreement based on 100k with sensitivity analysis evaluating agreement at 50k and 200k

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Explanatory variables

- Type of intervention (10 overlapping categories)
  - Care delivery, diagnostics, health education and promotion, immunization, medical devices, medical procedure, pharmaceutical, screening, surgical, other
- Disease category (12 overlapping categories)
  - Cancer, cardiovascular, digestive, endocrine, environmental, infection, musculoskeletal, mental health, maternal and perinatal, respiratory, sensory, other
- Funding source
  - Pharmaceutical industry vs other

Explanatory variables (2)

- Prevention stage
  - Primary: Methods used to prevent disease or illness
  - Secondary: Methods used to diagnose and treat disease in early stages before causing significant morbidity
  - Tertiary: Methods used to reduce negative impact of disease by restoring function and reducing disease-related complications
- Date of Study
  - Before 2005
  - 2005+

Analysis

- Assessment of percentage agreement for values of WTP between $0 and $200 (descriptive analysis)
- Bivariate comparisons of proportions of agreement (WTP=100k) by each of explanatory variables (unadjusted associations)
- Multivariable analysis of proportions of agreement (100k) with sensitivity analyses for 50k and 200k

Multivariable Logistic Regression for Agreement

- Estimate adjusted odds ratios for agreement
  - Odds ratios <1 indicate greater agreement than average
  - Odds ratios >1 indicate greater disagreement than average
- Because multiple cost-per-QALY ratios could be derived from a single study, for both bivariate and multivariable analysis we estimated robust standard errors clustered at the study level
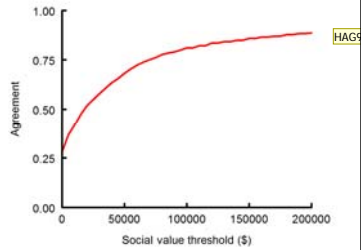
  Methods for cost analysis described later

HAG8   Are these all of the variables? What about disease burden and research intensity?
Henry Glick, 6/13/2012

Results

Percent Agreement

- 28% of time, com-paratively effective therapy was less expensive
- If WTP = 100k 81.1% of com-parisons agreed
- Thus, in 53.1% of comparisons (81.1-28.0), more effec-tive, more expensive therapy was comparatively effective
- In 18.9% (100-81.1) more effective, more expensive therapy comparatively effective but not cost-effective

(Chart: Agreement vs. Social value threshold ($), y-axis Agreement 0.00–1.00, x-axis 0–200000, labeled HAG9)

Unadjusted Agreement (100k), Overall and By Type of Intervention

	Agree	~Agree
Overall, N, (%)	1644 (81.1)	383 (18.9)
Type of intervention (NS)		
Most agreement		
Medical device	171 (86.8)	26 (13.2)
Other	52 (86.7)	8 (13.3)
Surgical	284 (86.1)	46 (13.9)
Least agreement		
Pharmaceuticals	745 (80.2)	184 (19.8)
Diagnostic	231 (79.1)	61 (20.9)
Screening (p=0.03)	258 (75.4)	84 (24.6)

HAG9   Are these all of the variables? What about disease burden and research intensity?
Henry Glick, 6/13/2012

Unadjusted Agreement, Disease Category

	Agree	~Agree
Disease category (p<0.05)		
Most agreement		
Other	264 (86.8)	40 (13.2)
Endocrine	138 (85.7)	23 (14.3)
Sensory	82 (85.4)	14 (14.6)
Least agreement		
Cancer	272 (78.2)	76 (21.8)
Respiratory	53 (77.9)	15 (22.1)
Musculoskeletal (p<0.002)	136 (69.0)	61 (31.0)

Unadjusted Agreement, Prevention Stage, Funding Source, and Year

	Agree	~Agree
Funding Source		
Pharmaceutical (p=0.000)	360 (91.6)	33 (8.4)
Other	1284 (78.6)	350 (21.4)
Prevention Stage (NS)		
Primary	291 (77.4)	85 (22.6)
Secondary	477 (80.7)	114 (19.3)
Tertiary	876 (82.6)	184 (17.4)
Year (NS)		
Before 2005	502 (80.6)	121 (19.4)
2005+	1141 (81.3)	263 (18.7)

Odds Ratios from 100k Agreement Logit *

Characteristic	OR	P-value
Type of intervention		
Surgery	1.90	0.02
Disease group		
Musculoskeletal	0.52	0.01
Pharmaceutical funding	3.35	0.000
Prevention stage		
Secondary	1.80	0.03

* >1 = more agreement; <1 = more disagreement; robust standard errors clustered at the article level

Sensitivity Analysis for 50k *

Characteristic	OR	P-value
Type of intervention		
Screening	0.62	0.04
Disease group		
Musculoskeletal	0.53	0.02
Pharmaceutical funding	2.23	0.000

- Surgery replaced by screening; secondary prevention no longer significant

* >1 = more agreement; <1 = more disagreement; robust standard errors clustered at the article level

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Sensitivity Analysis for 200k *

Characteristic	OR	P-value
Disease group		
Musculoskeletal	0.49	0.03
Pharmaceutical funding	2.71	0.003

- Neither surgery nor screening significant; secondary prevention remains insignificant

* >1 = more agreement; <1 = more disagreement; robust standard errors clustered at the article level

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Does adoption of most effective therapy reduce health care costs?

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Median Costs and QALYs

- Although mean costs and mean QALYs typically used in CEA, calculations rely on medians not means
- Do so because available data not optimal
  - Different studies have different Ns in denominator
  - Have different lengths of follow-up/projection

Agreement / Disagreement	%	Median Cost	Median QALYs	ICER of medians
Agree, Dominate	28	-$139	0.007	(Dominates)
Agree, ICER<100k	53.1	$2518	0.17	$14,811
Disagree	18.9	$3400	0.011	$309,100

- 32.5% of additional costs and 2.2% of additional QALYs derive from therapies where CER and CEA disagree

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Total Cost, Illustrative Calculation, $US 100k/QALY

- US population: 319 million
- Average prescriptions per capita: 2 (proxy for per-person volume of clinical choices of all types)
- Fraction of clinical choices with disagreement: 18.9%
- Median incremental cost when disagree: $3400
- Median QALYs gained when disagreement: 0.011
- Spending that would be avoided by not adopting comparatively effective, but not cost-effective therapies:
    319M * 2 * 0.189 x $3400 = $US 410 billion
- QALYs Lost
    319M * 2 * .189 * .011 = 1.3 million
- Cost/QALY: 410b / 1.3m = $US 309,100 / QALY

Discusion

Dominant Therapies

- In 28% of ratios, more clinically effective option was also lower cost
  - Would be preferred under any social value threshold/willingness to pay
- In 72 percent of ratios, more effective treatment was more costly
  - Unlikely that using all effective therapies will save money

Agreement

- At a willingness to pay of $US 100k, comparative effectiveness agreed with cost-effectiveness among 81.1% of ratios
  - 68% for 50k; 89% for 200k
- In majority of cases, clinicians will not have to override clinical judgments because of economic considerations

Predictors of Agreement

- Was some evidence of predictors of agreement / disagreement
- Most consistent predictors included:
  - Musculoskeletal diseases (less agreement)
  - Pharmaceutical funding (more agreement0
- Not clear that identification of these predictors allows us to adopt fewer musculoskeletal or more pharmaceutically funded studies without cost-effectiveness analysis

Increased Agreement for Pharmaceuticals

- Unsure what is causing, but
  - Might be result of well-targeted research funding
  - Selective publication of good clinical and cost-effectiveness results
  - Prior decisions to avoid development of relatively cost-ineffective treatments, or
  - Other reasons

Don't Have to Worry About Cost-Effectiveness?

- Although only 18.9% disagreement, there is possibly $US 400+ billion in costs year-after-year associated with these studies
  - Does 18.9% mean we don't have to worry about cost-effectiveness?
  - Does year-after-year 400+ billion in potential savings mean we can't rely solely on comparative effectiveness?
- Up to decision makers to decide

Limitations

- Had to rely on comparators chosen by authors
  - Not always assessing 2 most valuable Rx available
    - Possible to make therapy appear more/less favorable than it should
- Had to rely on published cost per QALY ratios
  - Published analyses need not be a random or representative sample of all analyses
- May represent a selected set of medical services
  - Those thought to be more (or less) cost-effective
  - Newer, more "high tech" therapies
- Limited to subset of studies that use QALYs as measure of comparative effectiveness
  - Minority of all comparative effectiveness studies

Uncertainty

- CEA Registry does not report variability of difference in costs or effects or of cost-effectiveness ratio
- Addition of variability generally thought to increase agreement
  - Point estimates indicate disagreement, but one or both estimates not significant (no significant difference in effectiveness or CI for CER that includes WTP) and we cannot be confident of disagreement
- But can decrease agreement
  - Point estimates indicate agreement, but nonsignificance of one or both estimates reduces confidence of agreement

Should PCORI Ignore Costs?

- PCORI Director's Rationale: PCORI should "put emphasis on clinical outcomes" and local public and private decision makers can develop economic evidence
  - Can't be efficient
  - Quality of evidence will be mixed at best
- Does development of clinical but not economic evidence make controlling costs harder rather than easier?
  - "But PCORI reported its most effective therapy...."
  - Future legislation?: "Insurers must cover most effective therapy as determined by PCORI"
- Should PCORI collect economic data, but not use it in making its recommendations?
  - Would increase efficiency and allow quality monitoring

Conclusions

- Large amount of agreement between comparative and cost-effectiveness
- Large cost possibly associated with Rx for which they disagree
- Unclear if study shows that we can stop performing / must perform cost-effectiveness analysis
- Many unknowns including:
  - How critical it is to reign in health care costs
  - Cost of performing cost-effectiveness analysis
    - Value of information analysis?
  - Political and "hassle" costs of rejecting use of effective, but cost-ineffective, therapies