

Expanding your Horizons: CER Continuing Education Certificate Program

July 30, 2014
2pm – 3pm, ET



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Implementation of the ICER Method at OmedaRx

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OmedaRx



Who is OmedaRx?

- Stand-alone PBM; owned by Cambia Health Solutions
 - Formerly RegenceRx
 - Affiliated with BlueCross BlueShield in Oregon, Utah; BlueShield in Washington, Idaho
- Provides formulary guidance & utilization management strategies to “Blues” and non-Blues plans nationwide
 - Medication Assessments
 - Medication Policies
 - P&T Committee Support

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Why Implement ICER?

- Challenges:
 - Consistent synthesis and application of critically-appraised literature.
 - Uniform lexicon for coverage conversations with stakeholders
- About ICER (Institute for Clinical and Economic Review)
 - Collaborative, nationally vetted
 - Aligns with current OmedaRx evaluation methods

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Implementation

- Extensive staff training
- Inservice to clients' P&T committees over multiple meetings
- Ongoing training
- Continuous quality improvement
- Decision tracking
- Developing custom formulary frameworks for each client

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The ICER Matrix (Previous version)

High Certainty	D (Inferior)	C (Comparable)	B (Small / Modest Benefit)	A (Moderate / Large benefit)
Moderate Certainty	I (Insufficient to determine)		P/I (Promising but Inconclusive)	
Low Certainty	I (Insufficient to determine)			
	Negative Health Benefit	Comparable Health Benefit	Incremental Health Benefit	Substantial Health Benefit

<http://www.icer-review.org/>

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OmedaRx ICER Process

Estimate
certainty in
the overall
clinical data

Estimate the
magnitude of
benefit
(based on
effectiveness)

Identify
"point
estimate" on
the ICER
matrix

Make safety
modification
to point
estimate

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Considerations for using the ICER Matrix

- Most reviews involve two comparisons :
 - against placebo
 - against existing therapies (if any)
- New therapies often lack direct comparative trials
 - Indirect comparisons
 - Compare the evidence synthesis of placebo-controlled data
 - The new HCV drugs are a perfect example
- Peer review
 - Staff consults with each other on our assessment of the evidence, our assessment of the standard of care, and our assessment of the safety profile
 - Improves inter-rater reliability

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Quantification of Effectiveness

<u>Certainty of Benefit</u>	<u>Definitions of Evidence (ICER)</u>	<u>Quantification of Studies (OmedaRx)</u>
High Certainty	Allows estimation for the relative potential chances / magnitude of net health benefit	≥ 1 high confidence study; consistent results OR ≥ 2 Fair confidence studies with: <ul style="list-style-type: none"> •Consistent results •Possibly clinically meaningful endpoint
Moderate Certainty	Difficult to estimate the net health benefit with precision	>1 high confidence study; inconsistent results OR ≥ 1 fair confidence study with: <ul style="list-style-type: none"> •Consistent results •Possibly clinically meaningful endpoint OR ≥ 2 low confidence studies with: <ul style="list-style-type: none"> •Consistent results •Possibly clinically meaningful endpoint
Low Certainty	Insufficient to allow assessment of the net health benefit	low confidence studies not meeting threshold for moderate certainty (defined above) OR ≥ 2 fair confidence studies with inconsistency in the results

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Estimate Health Benefit

High Certainty	D (Inferior)	C (Comparable)	B (Small / Modest Benefit)	A (Moderate / Large benefit)
Moderate Certainty	I (Insufficient to determine)		P/I (Promising but Inconclusive)	
Low Certainty	(Insufficient to determine)			
	Negative Health Benefit	Comparable Health Benefit	Incremental Health Benefit	Substantial Health Benefit

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Modify Point Estimate

Safety Conclusion Example	Estimate of Certainty	Estimate of Benefit
Track record with proven advantages (over active comparator)	← →	↑
Track record with no new safety concerns	← →	← →
Insufficient track record	↓	← →

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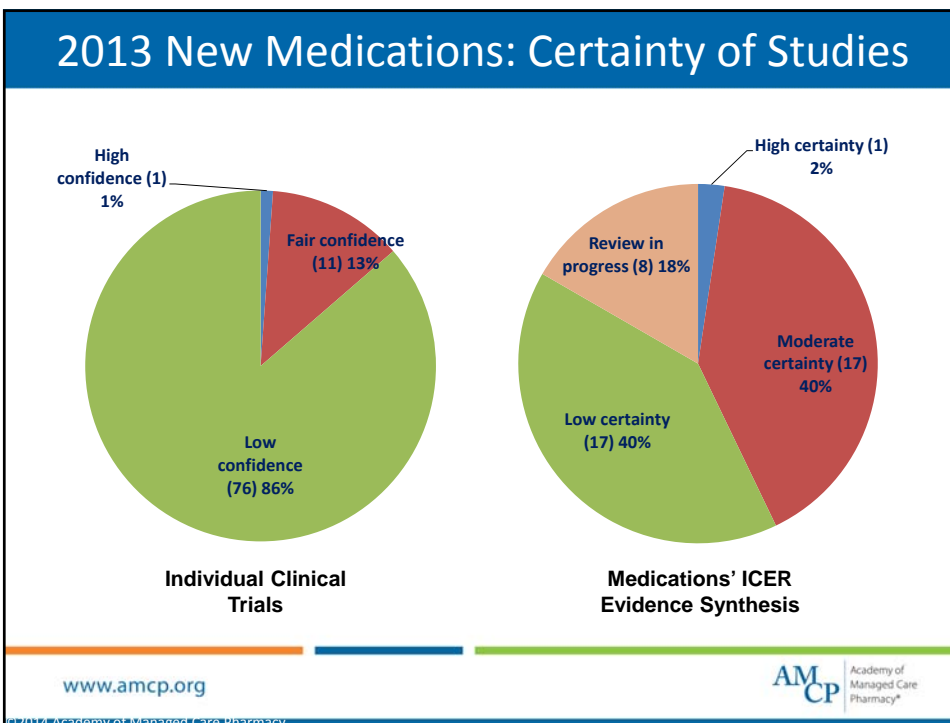
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Example Formulary Framework

MUST Prefer (Known clinical value)	MAY Prefer (Potential clinical value)	Do NOT Prefer (Unknown value/ harmful)
<p>A or B comparative evidence OR A or B non-comparative evidence AND no known difference in net health benefit vs comparable treatments</p> <p>(C, PI, or I comparative evidence) AND inter-patient variability in response to comparable medications warrants additional therapies</p> <p><u>Additional considerations</u> Cost proportional to clinical improvement (otherwise "May Prefer")</p>	<p>C, PI, or I comparative evidence AND At least PI non-comparative evidence</p> <p><u>"Must Prefer" if</u></p> <ul style="list-style-type: none"> • Significant, known inter-patient variability in response to comparable medications • Severity of disease warrants additional options 	<p>C, D, or I evidence</p>

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CER Collaborative ICER Graphic

The screenshot displays the CER Collaborative interface for the scenario "edogitran vs. warfarin". The main content is the "ICER Evidence Rating Matrix". The y-axis is labeled "Level of Certainty in the Evidence" and has four categories: High Certainty, Moderate Certainty, Low Certainty, and Insufficient. The x-axis represents the ICER Rating, with categories D, C, B, A, B+, C+, P/I, and I. A legend on the right defines these ratings: A: Superior, B+: Incremental or Better, B: Incremental, C+: Comparable or Better, C: Comparable, P/I: Promising but Inconclusive, D: Inferior, I: Insufficient. The matrix shows a rating of P/I at the Moderate Certainty level. The interface includes navigation buttons (Previous, Next, Save, Load, Clear) and a footer with the website "www.amcp.org" and the AMCP logo.

HCV: ICER and Models

- Votes California Technology Assessment Forum
 - “Evidence is adequate to demonstrate superiority of the new drugs with nuance for certain subpopulations and regimens
 - New drugs represent a “low value” to Medicaid health systems because the budget impact would displace other care and/or limit access”
- Beyond Budget Impact Models. CTAF model found:
 - “Cost to achieve 1 additional SVR with newer treatment regimens is greater than \$300,000
 - For every 1,000 patients treated, our model estimated that switching from previous standard treatments to the most effective new regimens in all patients would prevent 18 liver-related events over five years and 70 events over 20 years.
 - At a 5-year time horizon, however, cost offsets would still be estimated to represent less than 10-20% of upfront treatment costs.
 - Even at a 20-year horizon, if all patients infected with hepatitis C are treated with the new regimens, the cost offset will only cover approximately three-quarters of initial drug costs.”
- <http://www.ctaf.org/reports/treatments-hepatitis-c>

Lessons Learned

- Successful clinical evidence synthesis is dependent on rigorous evidence evaluation
- Agreed upon, uniform grading and synthesis guidelines are important for maintaining quality across multiple reviewers
- Quantification guidelines provide a basis for evidence description and discussion, not a replacement for professional judgement

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Expanding Your Horizons: CER Continuing Education Certificate Program

Second Generation of CER Decision Making

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July 30, 2014

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Overview – Second Generation CER

- Industry Dynamics
- What is CER?
- Why is CER necessary ?
- Approaches, methods, and tools
- Practical applications
- Building your foundation and skill sets

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Industry Dynamics

- Pharmaceutical pipeline is focused on biologics and specialty medications
 - Rare, complex conditions
 - High tech
 - Specialized care
- Due to the nature of rare, complex conditions, more and more medications are being approved based on data other than randomized, controlled studies
- Developing sound coverage policy
(e.g. transparent rationale and defensible criteria)

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What is CER?

- No single, standard definition
- Research that directly compares health care interventions to determine which is the most effective or can provide the best chances of positive health outcomes.
 - Compares benefits & harms of healthcare interventions
 - Identifies what works best when and for whom for informed decision making
 - Conducted in settings that are similar to those in which the intervention will be used in practice
 - Designed to measure improvement in health outcomes

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Second Generation CER – What is it?

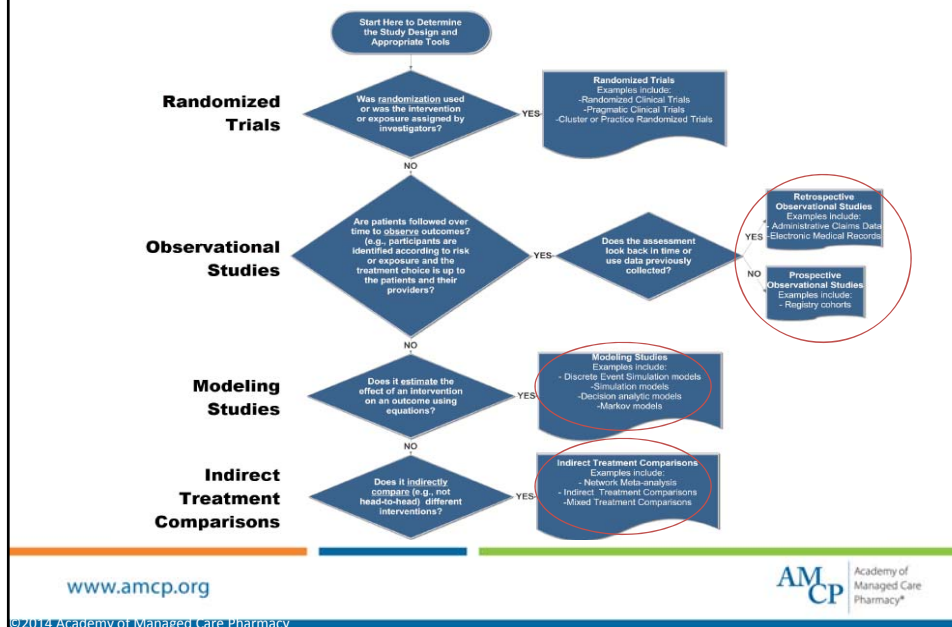
- Prospective observational studies
- Retrospective observational database studies
- Network meta-analysis/Indirect treatment comparison studies
- Modeling studies (PE, Budget Impact)

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Second Generation CER - What is It?



Value of Second Generation CER Why this is Needed?

- The elusive “Gold Standard RCT”
 - Specialty medications (accelerated approvals)
 - Rare Diseases
- Assessing risk/benefit in “real world conditions”.
- Greater depth in analyzing comparative effectiveness among similar medications (when head to head trials are lacking).
- Weighing the relative value of a medication on its potential to offset additional medical expenses, in the face of limited healthcare resources

Second Generation CER Implications for Industry

- Use familiar language of the decision-maker
- Ensure research meets good practice principles through eyes of reviewers
 - Consider when designing research
 - Review when finalizing publications
 - Consider when communicating evidence to decision-makers
- Training
- Dialogue, dialogue, dialogue

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CER Collaborative Tool

- Tools to evaluate second generation CER
 - Relevance
 - Credibility
- Critical appraisal/consistency in evaluation
- Synthesis of evidence
- Bottom line value conclusions a net health benefit (benefits & risks).

www.cercollaborative.org

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Critical Appraisal – Focus

Retrospective/ Prospective	Network Meta-analysis - Indirect Treatment Comparisons	Modeling
<ul style="list-style-type: none"> Design Data Analysis Reporting Interpretation Conflicts of Interest <ul style="list-style-type: none"> 33 items 	<ul style="list-style-type: none"> Evidence Base Analysis Reporting Interpretation Conflict of Interest <ul style="list-style-type: none"> 15 items 	<ul style="list-style-type: none"> Validation <ul style="list-style-type: none"> External Verification Face Design Data Analysis Reporting Interpretation Conflicts of Interest <ul style="list-style-type: none"> 26 items

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www.cercolaborative.org



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Practical Applications - Medication Review


Evolving Key Questions and Scope

<ul style="list-style-type: none"> Should sofosbuvir and/or simeprevir, two new medication treatments for HCV, be added to the formulary? 	<ul style="list-style-type: none"> How safe and effective are newer HCV medications (sofosbuvir and simeprevir) for the treatment of HCV? How do the safety and efficacy of these newer HCV medications (sofosbuvir and simeprevir) for chronic HCV compare to other HCV treatment options? 	<ul style="list-style-type: none"> What is the net health benefit (clinical risk/benefits) of sofosbuvir and simeprevir relative to older medication options for treatment of chronic HCV? 	<ul style="list-style-type: none"> What is the product value of newer HCV medications (simeprevir and sofosbuvir) for the treatment of chronic HCV? What is the comparative effectiveness of new HCV medications relative to existing HCV medications in various treatment regimens for chronic HCV genotypes? What is the potential <u>net health benefit</u> of newer HCV medications sofosbuvir and simeprevir (both clinically and <u>economically</u>) based on most current FDA approved indications and clinical practice guidelines?
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Basic ➔ Best Practice

“Greater depth and perspective for P and T Committee review.”

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Typical Way of Presenting Product & Cost Information

Regimens	Duration of Treatment	Estimated Cost per Treatment Course *
simeprevir triple therapy*	12 weeks triple therapy, then 12-36 weeks dual therapy	\$112,000-\$144,000
boceprevir triple therapy*	4 weeks dual therapy, then 24-44 weeks triple therapy	\$60,000-\$145,000
telaprevir (Incivek) triple therapy*	12 weeks triple therapy + 12-36 weeks dual therapy	\$112,000-\$144,000
sofosbuvir (Sovaldi) triple therapy* (e.g. Genotype 1 and 4)	12 weeks triple therapy	\$117,000
sofosbuvir (Sovaldi) + simeprevir (Olysio) + ribavirin (e.g. Genotype 1)	12 weeks therapy	\$184,584
sofosbuvir (Sovaldi) + simeprevir (Olysio) (e.g. Genotype 1, interferon ineligible patients)	12 weeks therapy	\$180,000
sofosbuvir (Sovaldi)-ribavirin (e.g. Genotypes 2 and 3; or Genotype 1 alternative for interferon ineligible patients)	12 weeks 24 weeks	\$106,000 \$207,000

*Price based on AWP (as of March 2014). Assumes use of peginterferon alfa-2a & 1,200 mg daily dose of ribavirin for triple therapy.

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Practical Application: Second Generation CER Provides More Depth in Articulating the Value Question

What is the potential net health benefit of newer agents (sofosbuvir and simeprevir) in treatment regimens for Hepatitis C in terms of their clinical benefit/risk potential and overall economic impact on health care costs relative to “older” HCV treatment regimens (e.g. boceprevir, teleprevir, peg-interferon/ribavirin)?

Conclusion

Newer agents (sofosbuvir, simeprevir) have superiority over older agents in HCV treatment regimens in achieving potential HCV cure (based on SVR) and improved safety; However, for most patient subpopulations, these new medications represent a low “product value” due to the magnitude of potential impact on health care costs and treating large numbers of patients for which there is uncertain cost-effectiveness (e.g. These medications did not show medical cost offsets (from avoiding down the road potential of liver complications) vs the cost of the medication regimen).

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Practical Applications Hepatitis C Treatment – Genotype 1

- No head to head trials of regimens incorporating simeprevir or sofosbuvir with the standard of care peg-interferon and ribavirin + either boceprevir or telaprevir
 - No head to head trials of regimens incorporating simeprevir or sofosbuvir with each other.
 - No trials with patient-oriented outcomes (decompensated cirrhosis, HCC, transplant, death).
- ↓
- Network meta-analysis performed using comparisons with peg-interferon/ribavirin (PR) to allow for indirect comparisons.
 - Modeling to estimate the economic impact and net offset with simeprevir and sofosbuvir.

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Summary of Benefits & Harms Hepatitis C by Prior Treatment Status and Interferon Eligibility

Treatment Approach (weeks)	SVR12 (Percent)	Treatment Burden	Adverse effects	Interferon -ineligible
Genotype 1				
Treatment-naïve				
PR (48)	47	48 weeks with weekly injections	Fatigue (50-60%), fever (40-45%), anemia (≤ 30%)	No
BOC[24] + PR[48]	73	Add Q8 pills	Anemia (≤ 50%), more nausea and dysgeusia, drug interactions	No
TVR[12] + PR[48]	74	Add Q8 pills	Anemia (≤ 50%), more nausea and pruritus, drug interactions	No
SMV[12] + PR[24-48]*	84	Add 1 pill to PR	No increase in anemia	No
SOF[12] + PR[12]	83	Add 1 pill to PR Fewer weeks	No increase in anemia	No
SMV[12] + SOF[12]	No data (Likely >90)	No P, maybe no R	Not reported yet	Maybe
Treatment-experienced				
PR (48)	22	48 weeks with weekly injections	Fatigue (50-60%), fever (40-45%), anemia (up to 30%)	No
BOC[24] + PR[48]	64	Add Q8 pills	Anemia (≤ 50%), more nausea and dysgeusia, drug interactions	No
TVR[12] + PR[48]	70	Add Q8 pills	Anemia (≤ 50%), more nausea and pruritus, drug interactions	No
SMV[12] + PR[24-48]*	70	Add 1 pill to PR	No increase in anemia	No
SOF[12] + PR[12]	No data (FDA estimate 71)	Add 1 pill to PR Fewer weeks	No increase in anemia	Maybe
SMV[12] + SOF[12]	90	No P, maybe no R	Not reported yet	Yes

Abbreviations: Q8 = taken every 8 hours; P = pegylated interferon; R = ribavirin
* Excluding patients with the Q80K mutation (approximately 10-15% of genotype 1 patients)

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Hepatitis C Treatments - Network Meta-Analysis

Estimates based on Clinical Trial Results

Clinical Trial Results for HCV Genotype 1 Treatment-Naive patients

Study	Treatment Arm	N	SVR12	SVR24
APACHE	SOV 120 QD + RBV + IFN	68	47%	52%
	SOV 120 QD + RBV + IFN	62	68%	68%
	SOV 120 QD + RBV + IFN	62	62%	62%
	SOV 120 QD + RBV + IFN	62	70%	70%
PRODIGE	SOV 120 QD + RBV + IFN	140	74%	74%
	PR2 + IFN	140	47%	47%
CONQUATOR	SOV 120 QD + RBV + IFN	140	77%	77%
	SOV 120 QD + RBV + IFN	74	54%	54%
CONVERTO 3	SOV 120 QD + RBV + IFN	38	70%	70%
	SOV 120 QD + RBV + IFN	38	58%	58%
CONVERTO 4	SOV 120 QD + RBV + IFN	55	71%	71%
	SOV 120 QD + RBV + IFN	55	51%	51%
ELECTRON	SOV 120 QD + RBV + IFN	102	80%	80%
	SOV 120 QD + RBV + IFN	102	50%	50%
COSMOS	SOV + SOV 120 + RBV	14	89%	89%
	SOV + SOV 120 + RBV + IFN	17	89%	89%
	SOV + SOV 120 + RBV + IFN	17	89%	89%
PILLMEDIK	SOV + SOV 120 + RBV + IFN	20	79%	79%
	SOV + SOV 120 + RBV + IFN	20	79%	79%

Summary Estimates from Network Meta-Analysis for SVR for Treatment-Naive Patients Infected with HCV Genotype 1

Treatment	SVR12	95% CI	P versus PR
PR	47%	41% to 52%	-
Boceprevir + PR	73%	68% to 77%	<0.001
Telaprevir + PR	74%	69% to 79%	<0.001
Simeprevir + PR*	84%	78% to 88%	<0.001
Sofosbuvir + PR	83%	79% to 87%	<0.001

* Excludes patients with the Q80K mutation

Clinical Trial Results for HCV Genotype 1 Treatment-Experienced Patients

Study	Treatment Arm	N	SVR12	SVR24
APACHE	SOV 120 QD + RBV + IFN	68	22%	29%
	SOV 120 QD + RBV + IFN	62	64%	64%
	SOV 120 QD + RBV + IFN	62	62%	62%
	SOV 120 QD + RBV + IFN	62	70%	70%
PRODIGE	SOV 120 QD + RBV + IFN	140	74%	74%
	PR2 + IFN	140	22%	22%
CONQUATOR	SOV 120 QD + RBV + IFN	140	77%	77%
	SOV 120 QD + RBV + IFN	74	24%	24%
CONVERTO 3	SOV 120 QD + RBV + IFN	38	70%	70%
	SOV 120 QD + RBV + IFN	38	58%	58%
CONVERTO 4	SOV 120 QD + RBV + IFN	55	71%	71%
	SOV 120 QD + RBV + IFN	55	51%	51%
ELECTRON	SOV 120 QD + RBV + IFN	102	80%	80%
	SOV 120 QD + RBV + IFN	102	50%	50%
COSMOS	SOV + SOV 120 + RBV	14	89%	89%
	SOV + SOV 120 + RBV + IFN	17	89%	89%
	SOV + SOV 120 + RBV + IFN	17	89%	89%
PILLMEDIK	SOV + SOV 120 + RBV + IFN	20	79%	79%
	SOV + SOV 120 + RBV + IFN	20	79%	79%


Summary Estimates from Network Meta-Analysis for SVR for Treatment-Experienced Patients Infected with HCV Genotype 1

Treatment	SVR12	95% CI	P versus PR
PR	22%	15% to 29%	-
Boceprevir + PR	64%	49% to 76%	<0.001
Telaprevir + PR	70%	61% to 77%	<0.001
Simeprevir + PR*	70%	58% to 79%	<0.001
Sofosbuvir + PR	?	?	?
Simeprevir + sofosbuvir (+ R)	90%	78% to 96%	<0.001

* Excludes patients with the Q80K mutation

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Hepatitis C Treatments - Network Meta-Analysis

- **Relevance - Sufficient**
 - Population Relevance – neutral
 - Intervention(s) missing - no
 - Outcome(s) missing - no
 - Setting/Circumstances applicable - yes
- **Credibility**
 - Validation - strength
 - Design – strength *Authors are transparent on assumptions and limitations*
 - Data – neutral/weakness. *Authors are transparent on limitations and holes in evidence for sofosbuvir (e.g. very little in the way of controlled study), thus some far-reaching assumptions for the network meta-analysis made. Therefore, some element of caution to exercise.*
 - Analysis - strength
 - Reporting - strength
 - Interpretation of results (fair/balanced) - strength
 - Conflict of interest - strength

AMCP Tool: “Sufficient” vs “Insufficient” to add to body of evidence”

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Second Generation CER Hepatitis C Treatments - Modeling

- **Relevance - Sufficient**
 - Population Relevance – neutral
 - Intervention(s) missing - no
 - Outcome(s) missing - no
 - Setting/Circumstances applicable - yes
- **Credibility**
 - Validation - strength
 - Design - strength
 - Data – neutral/weakness (conservative estimates of cost)
 - Analysis - strength
 - Reporting - strength
 - Interpretation of results (fair/balanced) - strength
 - Conflict of interest - strength

Model Overview

- Model of clinical and economic effects of sofosbuvir and simeprevir in hypothetical cohorts of 1,000 60-year-old newly-diagnosed
- Control status
- Prevalence
- Outcome
- Region
- Finding

Analyses of Budget Impact in California

- Size of infected population estimated using published estimates from NHANES and other sources
- Impact
- Add
- Subtract
- Total
- Cost
- Offsets
- Net
- No
- Of
- Cost
- Effect

Key Assumptions

- Full compliance with and completion of therapeutic regimen
- Cost per SVR and downstream cost offsets based on effectiveness of initial course of therapy only
- Clinical benefits limited to SVR and its effects on downstream liver-related outcomes


Model Limitations

- Insufficient data for quantitative synthesis in many cases, reliance on individual study estimates
- Assumed perfect compliance with and completion of drug regimens
- Clinical effects and costs of drug-related adverse effects not considered
- Other benefits of treatment (e.g., improved quality of life, work/school productivity) not measured

Tice JA et al. The comparative clinical effectiveness and value of simeprevir and sofosbuvir in the treatment of chronic hepatitis infection. A technology assessment. Final report. Institute for Clinical and Economic Review. April 15, 2014

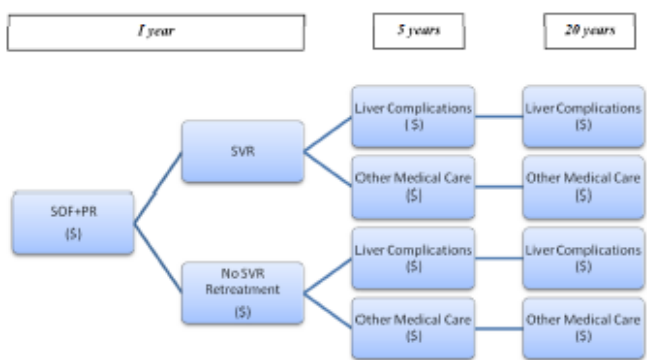
AMCP Tool: “Sufficient” vs “Insufficient” to add to body of evidence”

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Modeling: Depicting of Model Flow



SOF: Sofosbuvir; PR: Pegylated Interferon + ribavirin; SVR: Sustained virologic response

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Modeling - HCV Genotype 1 (Treatment Naïve) Cost Per SVR & Total Cost Offsets vs "Usual Care"

Population/regimen	Evidence Review Data					Modeled 1-Year Drug Costs		Modeled Long-Term Effects of Achieving SVR			
	SVR per 1000	NNT for 1 add'l SVR	Discontinued due to AE (per 1000)	Cost for initial Rx (per patient)	Cost per add'l SVR	Total Drug Costs (per 1000)	Incremental (vs. pre-DAA)	Liver Events Averted 5 years (per 1000)	Liver Events Averted 20 years (per 1000)	Total Estimated Cost Offset 5 years (per 1000, vs. pre-DAA)	Total Estimated Cost Offset 20 years (per 1000, vs. pre-DAA)
IFV-eligible											
TEL + PR (12/24) (pre-DAA)*	740	---	140	\$83,976	---	\$107,712,960	---	---	---	---	---
SMV + PR (12/24)*	840	10	64	\$91,296	\$73,000	\$105,903,360	(\$1,810,000)	(5)	(19)	(\$2,393,000)	(\$7,730,000)
SOF + PR (12)*	830	11	55	\$96,468	\$139,000	\$111,988,320	\$4,275,000	(4)	(17)	(\$2,154,000)	(\$6,957,000)
IFV-ineligible											
No Rx (pre-DAA)	0	---	0	\$0	---	\$0	---	---	---	---	---
SOF + R (24)†	720	1	13	\$176,352	\$245,000	\$219,622,080	\$219,622,000	(35)	(138)	(\$17,233,000)	(\$55,653,000)
SOF + SMV + R (12)‡	900	1	0	\$154,536	\$172,000	\$169,989,600	\$169,990,000	(43)	(173)	(\$21,541,000)	(\$69,566,000)

*ICER network meta-analysis
 †DAA estimate based on data from NEUTRINO among patients with "poor prognostic factors"
 ‡Pooled data from COSMOS treatment arms
 †††No available data. Data pooled from PHOTON-1 and QUANTUM and adjusted downward based on decrement from Rx-naïve to Rx-experienced with SOF4PR (83% vs. 71%)
 Total drug costs include initial therapy and retreatment with most effective regimen available for those not achieving SVR initially
 Total estimated cost offset includes cost savings from liver events averted and reduced annual costs from greater numbers of patients achieving SVR
 N/C: Not calculable
 SVR: sustained virologic response; NNT: number needed to treat; DAA: direct-acting antivirals

No cost offset estimated at 5 years or at 20 years.

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Tice JA et al. The comparative clinical effectiveness and value of simeprevir and sofosbuvir in the treatment of chronic hepatitis infection. A technology assessment. Final report. Institute for Clinical and Economic Review. April 15, 2014.



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Modeling – HCV Genotype 1 (Treatment- Experienced) Cost Per SVR & Total Cost Offset

Population/regimen	Evidence Review Data					Modeled 1-Year Drug Costs		Modeled Long-Term Effects of Achieving SVR			
	SVR per 1000	NNT for 1 add'l SVR	Discontinued due to AE (per 1000)	Cost for initial Rx (per patient)	Cost per add'l SVR	Total Drug Costs (per 1000)	Incremental (vs. pre-DAA)	Liver Events Averted 5 years (per 1000)	Liver Events Averted 20 years (per 1000)	Total Estimated Cost Offset 5 years (per 1000, vs. pre-DAA)	Total Estimated Cost Offset 20 years (per 1000, vs. pre-DAA)
IFV-eligible											
TEL + PR (12/24) (pre-DAA)*	700	---	140	\$83,976	---	\$130,336,800	---	---	---	---	---
SMV + PR (12/24)*	700	N/C	64	\$91,296	N/C	\$137,656,800	\$7,320,000	0	0	\$0	\$0
SOF + PR (12)*	710	100	55	\$96,468	\$1,249,000	\$141,383,440	\$10,947,000	(0)	(2)	(\$239,000)	(\$773,000)
SOF + SMV + R (12)‡	900	5	0	\$154,536	\$353,000	\$169,989,600	\$39,653,000	(10)	(38)	(\$4,787,000)	(\$15,459,000)
IFV-ineligible											
No Rx (pre-DAA)	0	---	0	\$0	---	\$0	---	---	---	---	---
SOF + R (24)†	610	2	13	\$176,352	\$289,000	\$236,621,040	\$236,621,000	(29)	(117)	(\$14,600,000)	(\$47,150,000)
SOF + SMV + R (12)‡	900	1	0	\$154,536	\$172,000	\$169,989,600	\$169,990,000	(43)	(173)	(\$21,541,000)	(\$69,566,000)

*ICER network meta-analysis
 †DAA estimate based on data from NEUTRINO among patients with "poor prognostic factors"
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Second Generation CER Hepatitis C Treatments – Payer Decision-making

Conclusions

- Newer agents (sofosbuvir, simeprevir) have superiority over older agents in HCV treatment regimens in achieving potential HCV cure (based on SVR) and improved safety;
- However, for most patient subpopulations, these new medications represent a low “product value” due to the magnitude of potential impact on health care costs and treating large numbers of patients for there is uncertain cost-effectiveness (e.g. Medical cost offsets from avoiding down the road liver complications versus cost of medication drug regimens).

Implications

- Create UM coverage criteria that is transparent for when certain medication regimens are covered (e.g. genotype, naïve vs retreatment, urgent treatment need (e.g. liver fibrosis stage), and documented contraindication or previous intolerance of peg-interferon.
- Avoid “tried/failed” language; or “silent” policy criteria.

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Foundation - What's Needed for Success

- Organizational philosophy
- Investment in training skills of pharmacist in assessing these types of studies/data.
- Practice in scoping and assimilating of “evidence”.
- P and T Committee training (Charter update)
- Consistency/transparency (inter-rater reliability)

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Decision Making: CER in Action

Element	Description
Overall Operational Strategy (Discovery Phase)	Baseline assessment that includes identified areas of opportunities for process improvement and recommendations for new or modified approach in drug evaluation review process.
Brand/Specialty Pipeline Tracking	What are processes for medication pipeline tracking and dissemination of drug information on drugs new market.
Generic Pipeline Tracking	Medication pipeline tracking and dissemination of drug information on drugs new market.
Brief Drug Overviews (Snapshots)	Incorporate process enhancements and refine documents used to announce information about newly approved medications and preliminary utilization management recommendations.
Drug Review Monograph	Update/Revamp of the Drug Evaluation Monograph and/or additional sections or information needed to address best practice approaches of tools provided by the CER collaborative. Embed triggers for staff that encourage scoping that includes second generation CER, based on PICOT questions.
Staff Training Support	Provide initial and ongoing training support for clinical staff in the implementation & application of tools, with guidance on continuous process improvement to gain greater efficiencies and consistency in the incorporation of new tools.
Quality Metrics/Auditing Quality/Audit	Work provided/Deliverable: Assist with tool development and process to routinely and objectively track/assess EBM Evaluation Program (quality, inter-rater reliability, timeliness, additional staff training needs).

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Next Steps – Developing your CER Tool Kit

- Key Questions (PICOT)
- Search Strategy & Documentation
- Evidence Tables & Critical Appraisal
 - Primary Literature
 - Secondary Literature
 - **Prospective/Retrospective observational studies**
 - **Network meta-analyses/Indirect treatment comparisons**
 - **Modeling studies (Value, Cost effectiveness)**
 - **AMCP Dossier**
- Evidence Synthesis – ICER (Value Statement)
- National Practice Guidelines / Expert Opinion

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Next Steps

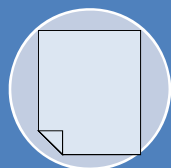
- Build foundation for CER (primary/secondary literature).
- Expand scope of medication reviews that encourage the inclusion of these types of studies.
- Start small by focusing on key classes to gain experience and familiarity with tools.
- Implement quality assurance/improvement process.

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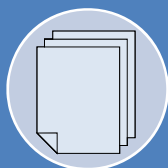
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AMCP/ISPOR/NPC CER Collaborative



Part 1: Evaluate Quality of Individual Studies

- Prospective
- Retrospective
- Modeling
- Indirect Methods



Part 2: Synthesizing the Evidence Across Multiple Study Types

- RCT, Observational studies



Part 3: Assessing the Evidence by Decision Makers: A Toolkit

- Tools
- Educational Materials and Training

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CER Collaborative Certificate Program

Module 6
New
Webinar
Option!

Module 6 Skills Demonstration

Live at Nexus/Annual or **NEW** Webinar Option

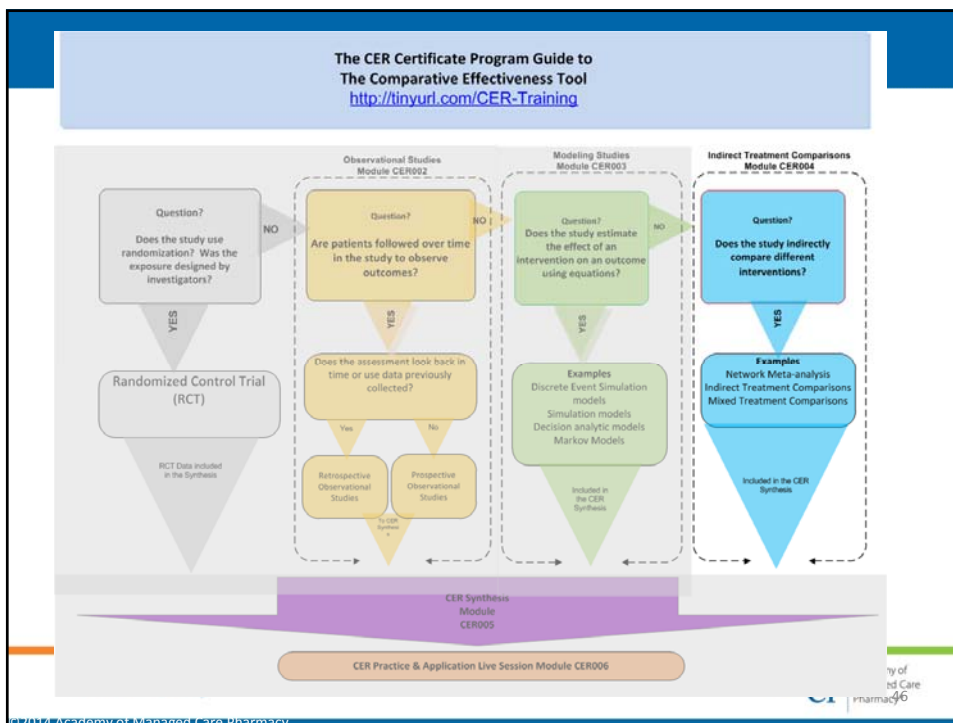
- Complete Modules 01 to 05
- Register for Module 06W – web version
- Complete Pre-Meeting Assignment
- Complete Module 6 Webinar –a 4 hour webinar:
 - Segment 1 (30 minutes): Full Class Meeting for Introductions and Instructions
 - Segment 2 (60 minutes): Individual Case Presentations
 - Segment 3 (60 minutes): Group Assignment
 - Segment 4 (90 minutes): Full Class Meeting for Group Presentations




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CER Certificate Program

http://www.pharmacists4knowledge.org/cips/cer

The screenshot shows a web browser displaying the CIPS Knowledge Enterprise website. The page features a navigation menu with links for Home, About Us, Courses, FAQs, Blog, Contact Us, and Join. The main content area is divided into two columns. The left column, titled 'Course Detail', provides information about the 'AMCP Members: Comparative Effectiveness Research Certificate Program', including credit hours (19.0 Contact Hours) and fees (\$895.00 for members, \$400.00 for students). It also mentions the 'CER Collaborative' involving AMCP and the National Pharmaceutical Council, and states the program is available starting April 1st. The right column, titled 'Course Listings', lists various topics such as 'Respiratory Drug Delivery Tools', 'Essentials of Rx for Asthma', and 'Pharmacologic Management of Dyslipidemia'.

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How to Ask A Question

The screenshot shows a GoToWebinar interface. On the left, there is a vertical toolbar with icons for audio, chat, and other functions. The main window displays audio settings, including a 'MUTED' indicator and a volume slider. Below the audio controls is a 'Questions' section with a text input field containing the placeholder text '[Enter a question for staff]' and a 'Send' button. Two arrows point to the 'Raise your hand' icon in the toolbar and the 'Questions' input field, with accompanying text: 'Raise your hand to ask verbally' and 'Or, type your question in the 'Questions' area'. At the bottom of the window, it shows 'Now Webinar ID: 158-614-635' and the 'GoToWebinar' logo.

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