EVIDENCE FOR MEDICARE

ADVI

A Perspective on Medicare
Louis Jacques MD

FDA GI

July 29, 2016

Social Security Act 1862(a)(1)

Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services—

(A) which, except for items and services described in a succeeding subparagraph or additional preventive services (as described in section 1395x(ddd)(1) of this title), are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member,

***

(E) in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section,

***

ADVI

What is the definition of R&N?

- Congress did not define it.
- HCFA attempted unsuccessfully to define via rulemaking in ‘89 and ‘00.
- CMS explored attempting rulemaking again, but there was no traction.
- For practical uses, CMS has operationalized the following definition:

Adequate evidence to conclude that the item or service improves clinically meaningful health outcomes for the Medicare population

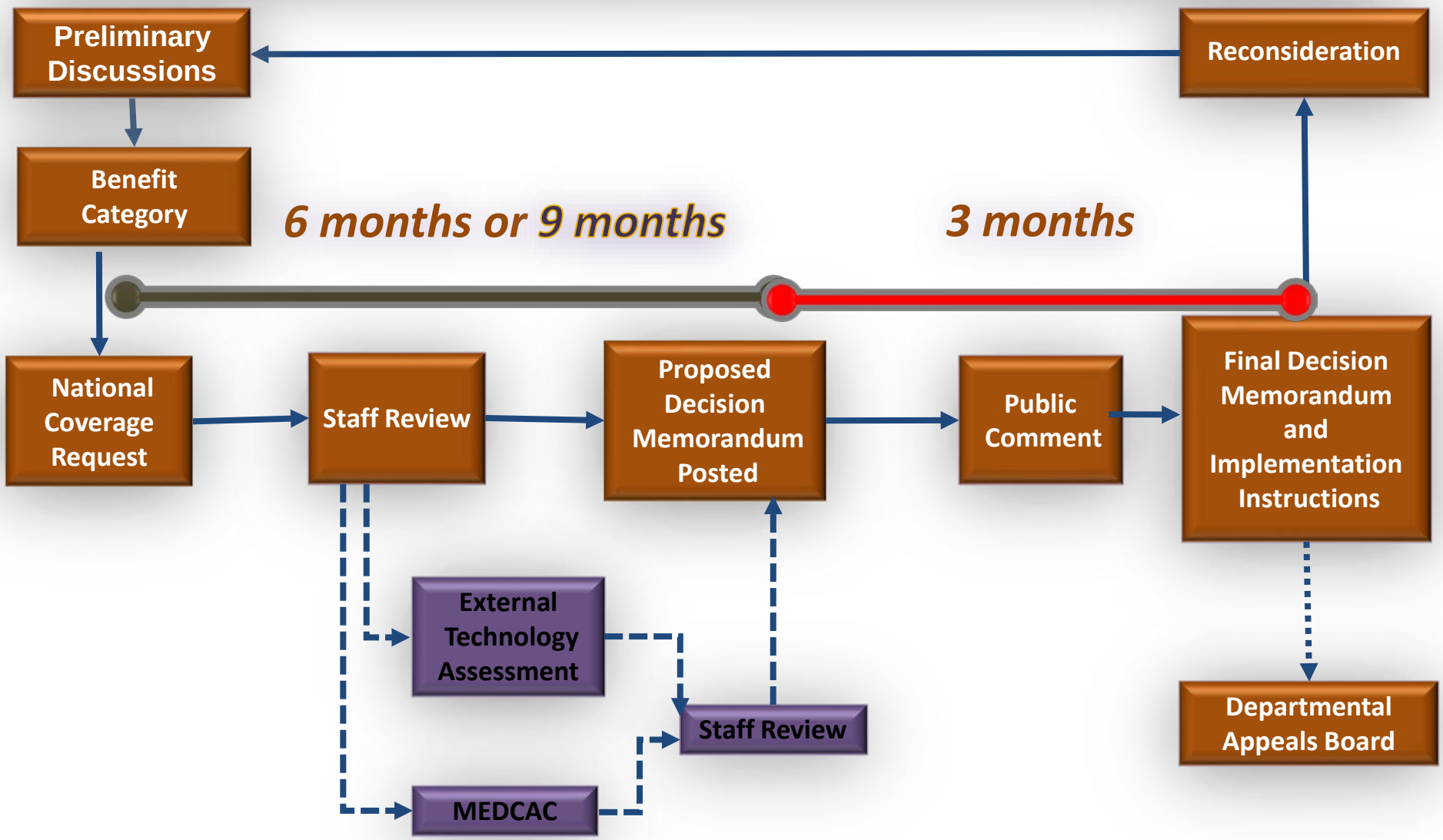
ADVI

Medicare Fee for Service

- Most decisions are deferred to local administrative contractors (MACs).
- The claims system defaults to payment if the code is not edited for nonpayment or suspension.
- Payment amounts determined by Congressional formulae.

ADVI

MEDICARE NATIONAL COVERAGE PROCESS



ADVI

The Preferred Road to Therapeutic Coverage

- ✓ Provide adequate evidence that
- ✓ A treatment strategy using the new therapeutic technology compared to alternatives
- ✓ Leads to improved clinically meaningful health outcomes
- ✓ In Medicare beneficiaries

ADVI

General Methodological Principles of Study Design (Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

ADVI

Common Concerns

- Inadequate randomization, blinding, controls
- Unrealistic comparators
- Intermediates/surrogates don’t map rigorously to clinical utility outcomes
- Composite outcomes with asymmetry btwn arms
- Lack of generalizability to typical targeted Medicare beneficiary
- Conflicts of interest
- Bad results get buried

ADVI

Comparison of Effects as Evidence Evolves From Single Trials to High-Quality Bodies of Evidence

Structured Abstract

Objective. The objective of our methods project was to use a diverse sample of medical interventions to assess empirically whether first trials rendered substantially different treatment effect estimates than reliable, high-quality bodies of evidence.

Study design and setting. We employed a meta-epidemiological study design using 100 bodies of evidence from Cochrane reports that had been graded as high quality of evidence. To determine the concordance of effect estimates between first and subsequent trials, we applied both quantitative and qualitative approaches. For quantitative assessment, we used Lin's concordance correlation and calculated z-scores; to determine the magnitude of differences of treatment effects, we calculated standardized mean differences (SMDs) and ratios of relative risks. We determined qualitative concordance based on a 2-tiered approach incorporating changes in statistical significance and magnitude of effect.

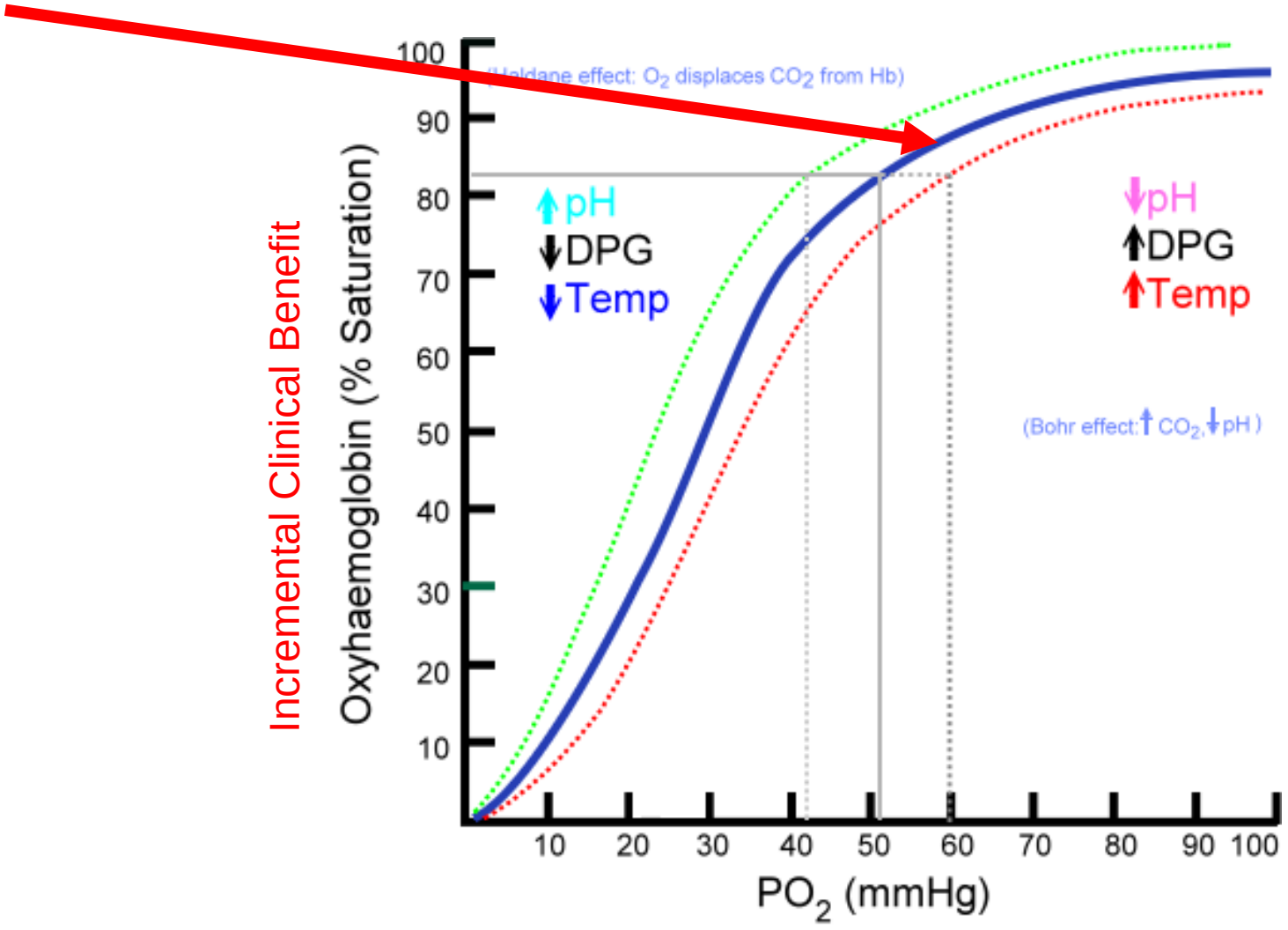
Results. First trials both over- and under-estimated the true treatment effects in no discernible pattern. Nevertheless, depending on the definition of concordance, effect estimates of first trials were concordant with pooled subsequent studies in at least 33 percent but up to 50 percent of comparisons. The pooled magnitude of change as bodies of evidence advanced from single trials to high-quality bodies of evidence was 0.16 SMD (95% confidence interval [CI], 0.12 to 0.21). In 80 percent of comparisons the difference in effect estimates was smaller than 0.5 SMDs. In first trials with large treatment effects (>0.5 SMD), however, estimates of effect substantially changed as new evidence accrued (mean change 0.68 SMD, 95% CI, .50 to 0.86)

Conclusion. Results of first trials often change but the magnitude of change, on average, is small. Exceptions are first trials that present large treatment effects which often dissipate as new evidence accrues.

http://www.effectivehealthcare.ahrq.gov/ehc/products/549/2057/grades-predictive-values-evidence-150331.pdf

ADVI

You Are Here



Clinical Trial Size and Duration

ADVI

The Plumbing Paradigm of Progress in Revascularization

1. How many plugged drains do you need to study to prove that the red one is better than the blue one?

2. If the red one costs 4X as much as the blue one, how much better does it have to be for you to buy it?

3. Suppose you already have a blue one at home?

ADVI

The Challenges of Non-Inferiority

Why would CMS prefer superiority trial designs to inform coverage?

- Derivation of the delta
- Clinical creep – inferiority to placebo
- Assay sensitivity – bias toward N-I
- Blinding vulnerability– bias toward N-I

"Mrs. Jones, I am 80 percent confident that this new treatment is no more than 15 percent worse that what we would have done last year."

ADVI

Don’t Do Any of These…

- Exclude enrollment of subjects > 65 years old, unless disease is generally only found in younger patients.
- Exclude adequate numbers of women, unless the disease is in men only or the treatment would be inapplicable to women.
- Exclude subjects with comorbidities commonly found in the relevant beneficiary population.
- Tell different stories to FDA and CMS

ADVI

POLICY, REGULATION & ETHICS

PERSPECTIVE

Medicare coverage: engaging on evidence

Tamara Syrek Jensen & Louis B Jacques*

Experience tells us that many developers of innovative technologies fail to anticipate the evidentiary needs of insurers, particularly of Medicare. Some assume that Medicare payment begins *pro forma* upon approval or clearance by the US FDA with little regard to the distinct role of the Centers for Medicare & Medicaid Services (CMS). We offer our own suggestions, hoping they will lead to mutually satisfying discussions as we consider coverage of regenerative medicine technology. Medicare is governed by Title XVIII of the Social Security Act, which among other provisions describes the scope of the insurance benefit, methods of payment for items and services that may be covered and the process timelines for national coverage determinations. CMS implements these provisions with regulations, instructions in manuals and other guidance that are available to the public. We will focus our comments on the 'reasonable and necessary' requirement for coverage under Part A and Part B of items and services in Section 1862(a)(1)(A) of the Social Security Act.

Jensen, TS, Jacques LB. Medicare coverage: engaging on evidence. Regenerative Medicine, Vol. 6, No. 6s, November 2011: 99-101.

ADVI

The Preferred Road to Diagnostic Coverage

- ✓ Provide adequate evidence that
- ✓ The incremental information obtained by new diagnostic technology compared to alternatives
- ✓ Changes physician recommendations
- ✓ Resulting in changes in therapy
- ✓ That improve clinically meaningful health outcomes
- ✓ In Medicare beneficiaries

ADVI

42 CFR 410.32

(a) *Ordering diagnostic tests.* All diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Tests not ordered by the physician who is treating the beneficiary are not reasonable and necessary (see § 411.15(k)(1) of this chapter).

ADVI

Medicare

- EGAPP – ACCE criteria have been endorsed at multiple MEDCACs
- Seek evidence based chain of logic to find clinical utility
- Few national decisions – PGx for warfarin response (2009)
- Mostly MAC policies – MolDx pilot
- FDA review if applicable (*per FDA*)
- Coding and payment issues

ADVI

Desirable Evidence

We often get

We cope with

We really want

Diagnostic Imaging Evidence Hierarchy Level	Genetic Testing Evidence Category	Example of Outcome Measures
1. Technical Efficacy	1. Analytic validity	Interpretable scan resolution, accuracy and reliability of tests of CSF proteins to measure CSF protein levels, inter-reader and inter-laboratory reliability of test results
2. Diagnostic Accuracy	2. Clinical validity	Sensitivity/specificity vs. gold standard test or vs. some other standard
3. Diagnostic Impression		Change in presumptive diagnosis following introduction of new test results
4. Diagnostic Action		Initiation or cessation of treatment; impact on use of additional diagnostic studies
5. Patient Outcomes	3. Clinical utility	Cognitive/functional decline, time to institutionalization, side effects of treatment driven by test results, mortality
6. Societal Outcomes		Cost-effectiveness of testing

ADVI

Louis B. Jacques, MD
SVP & Chief Clinical Officer,
ADVI

ADVI.COM
202 509 0760

1050 K St, NW
Suite 340
WASHINGTON, DC 20001

Louis.Jacques@ADVI.COM

ADVI