Assessing Genomic Sequencing Information for Health Care Decision Making

Decision Making Once Evidence is Assessed/Graded Evaluated

Guideline Development
The American Society of Clinical Oncology

Gary Lyman, MD, MPH, FASCO

Hutchinson Institute for Cancer Outcomes Research

Fred Hutchinson Cancer Research Center

University of Washington, Seattle, WA

FRED HUTCHINSON CANCER RESEARCH CENTER

HICOR

Hutchinson Institute for Cancer Outcomes Research

12


SEAHAWKS
SUPER BOWL
XLVIII
BRONCOS
SUPER
BOWL
BOUND

Genomic-Driven Cancer Medicine

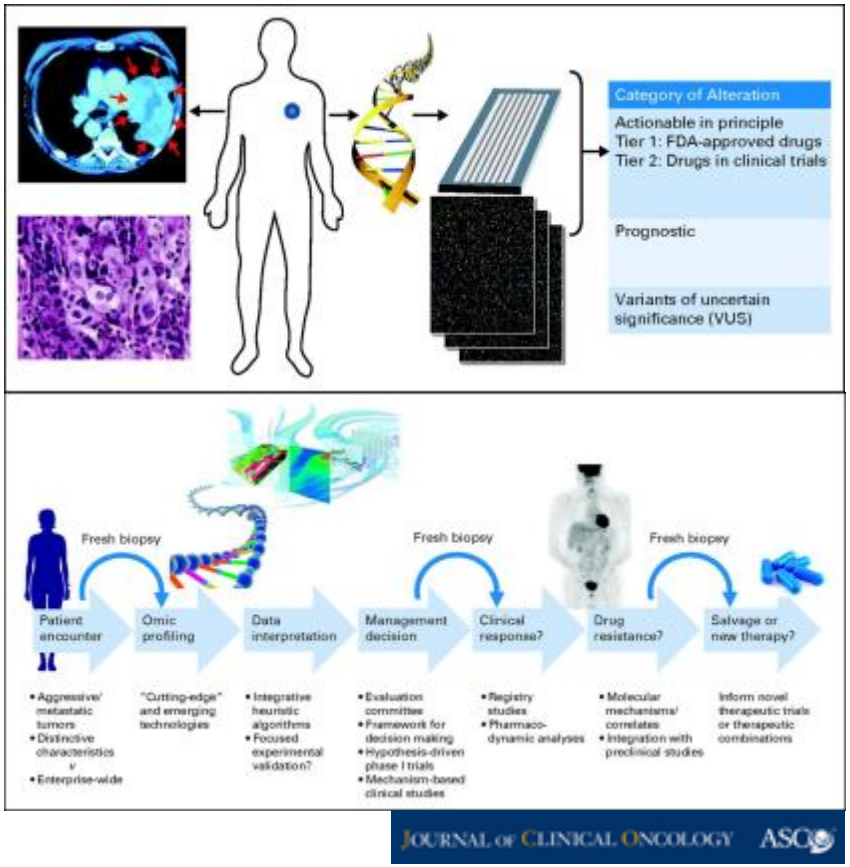
Overarching Questions

Question 1: *Which mutational profiling approaches will be most enabling for genomics-driven cancer medicine?*

Question 2: *What interpretive frame-works may render complex genomic data accessible to oncologists?*

Question 3: *What clinical trial designs will optimally evaluate the utility of tumor genomic information?*

Question 4: *How will oncologists and patients handle the return of large-scale genomic information?*



Garraway L A JCO 2013;31:1806-1814

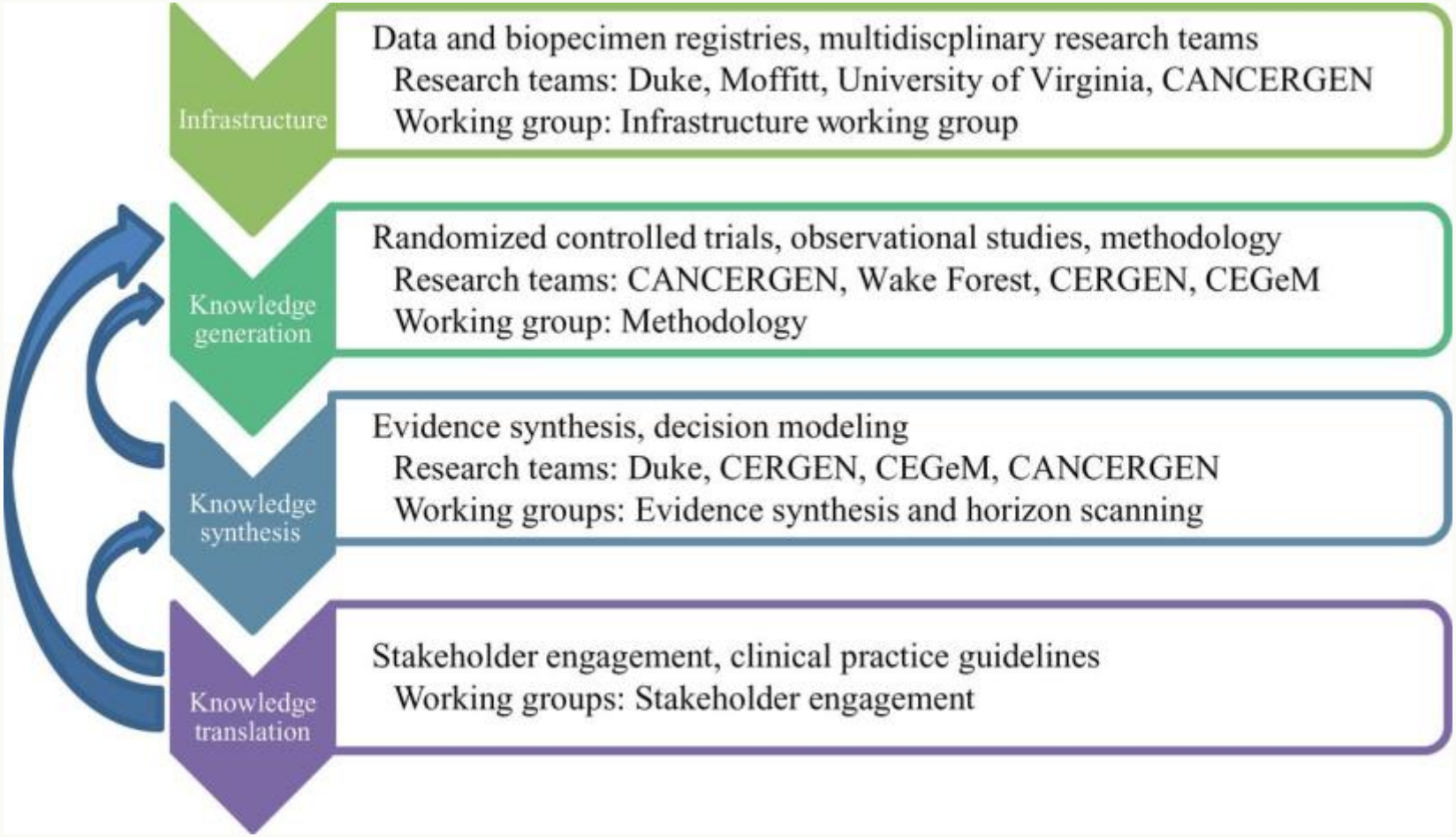
Genomic-Driven Cancer Medicine

"...oncology has served as a proving ground for the genomics-driven framework that is unique among medical specialties."

"A well-recognized pitfall of genomics-driven cancer medicine centers on the risk that large-scale genomic data generation could emerge without an evidence-based clinical approach to data analysis and interpretation."

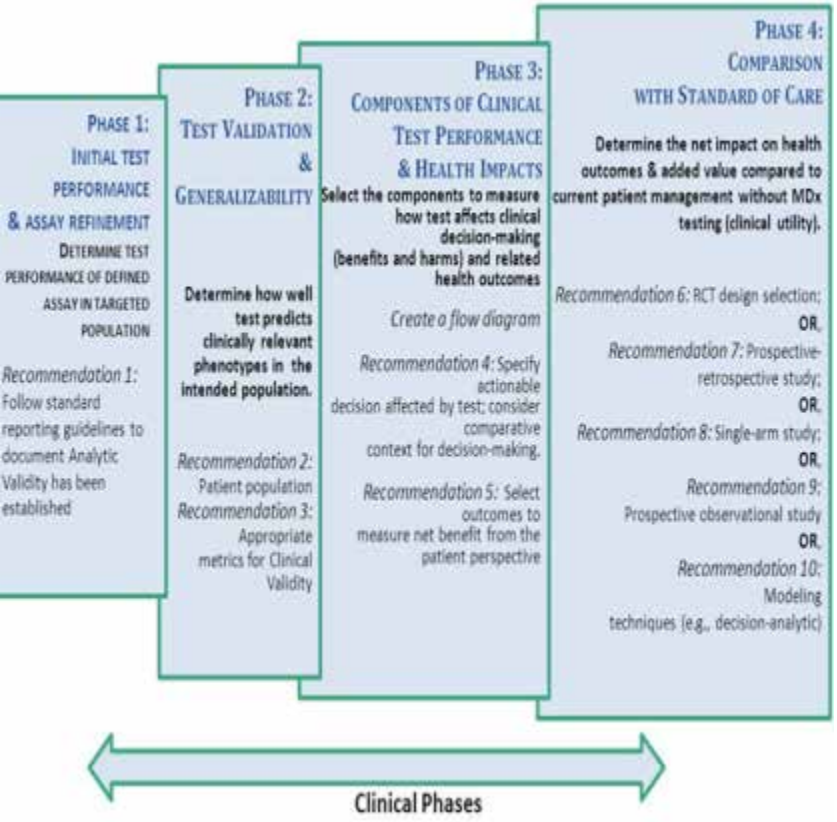
Garraway L A JCO 2013;31:1806-1814

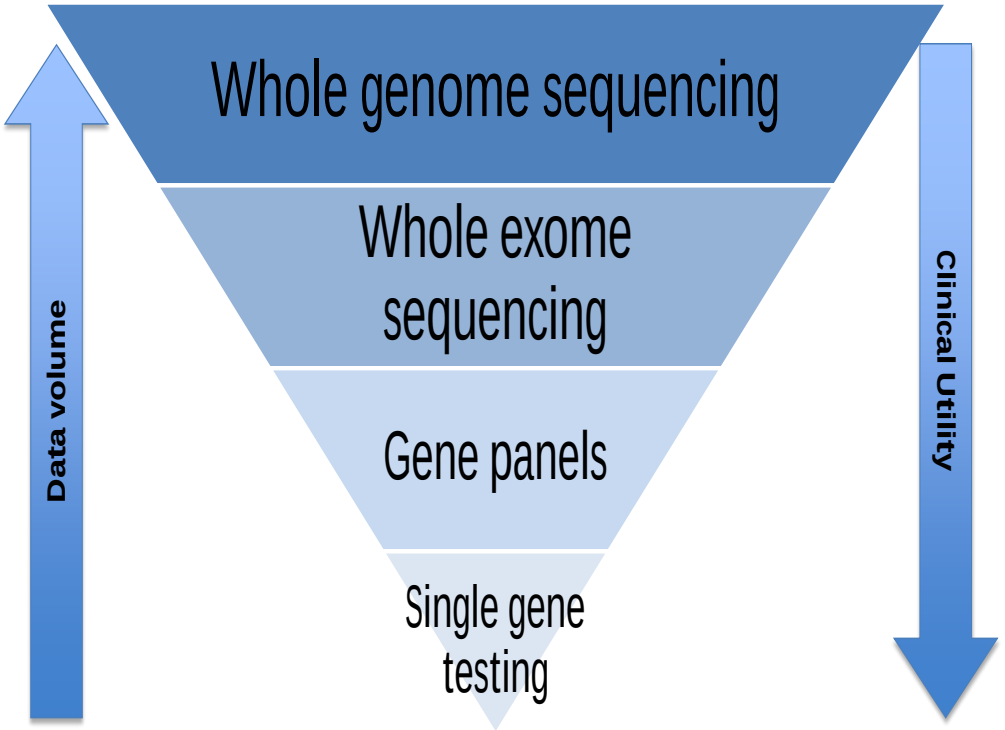
Comparative Effectiveness Research in Cancer Genomics and Precision Medicine: *Landscape and Future Prospects*



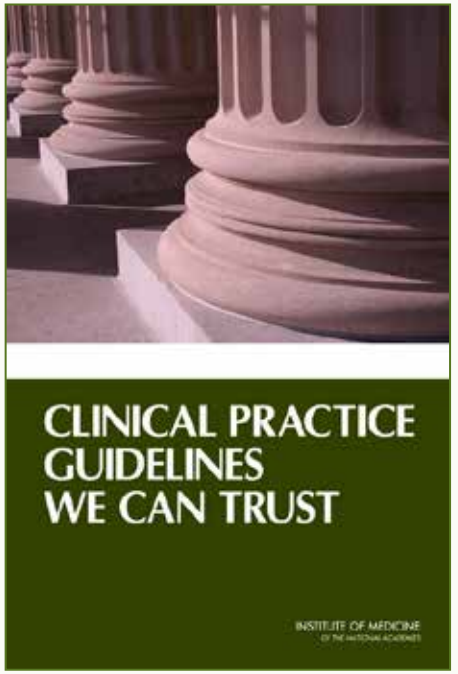
Simonds N I et al. JNCI 2013; 105: 929-936

CMTP EVIDENCE GUIDANCE DOCUMENTS
ACTIONABLE DIAGNOSTIC TESTS AND BEYOND





Institute of Medicine Standards



1. Transparent process
2. COIs managed/disclosed
3. Multidisciplinary expert panels
4. Based on rigorous systematic reviews
5. Ratings for strength of evidence and strength of recommendations
6. Standardized and clear recommendations
7. External review including public comment
8. Updating plan

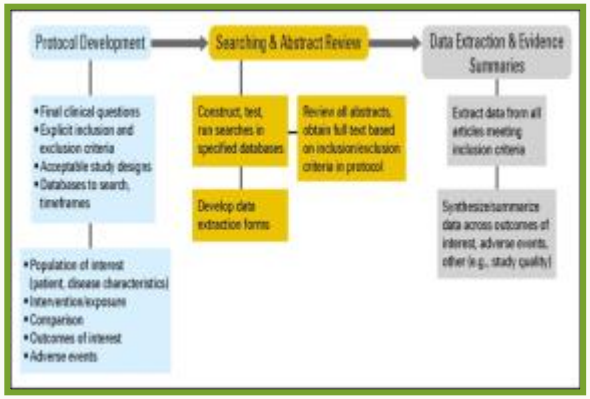
ASCO Clinical Practice Guidelines

Complex Development Process

Topic selection
Appoint Steering Comm.
Define relevant questions
Explicit Inclusion/Exclusion

Identify Co-Chairs
Assemble panel
Manage COIs

Systematic Review → **Guideline Development** → **Dissemination**



Review of evidence
Generate recs
Multiple internal & external reviews

JCO/JOP
PGIN
ASCO.org
Quality Measures/QOPI

ASCO GUIDELINES
Clinical Tools and Resources

ASCO Guideline Development Process

Methodological Challenges

VALIDITY
"ideal"

- Methodologically rigorous
- Complies with IOM
- Capitalizes on expert ASCO volunteers
- Strict COI policy

EFFICIENCY
"Expedient"

- Inefficient workflow
- Low output
- Relies on volunteers
- Often requires a "champion"

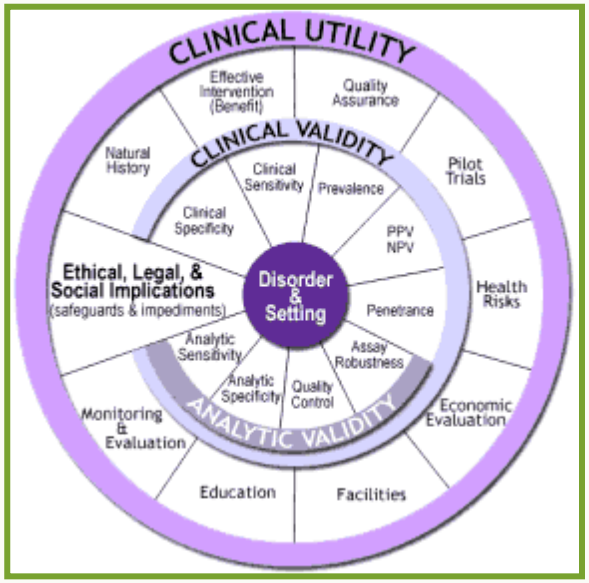
Published ASCO Biomarkers Guidelines

- Use of tumor marker tests in the prevention, screening, treatment, and surveillance of **breast cancer**
- ASCO/CAP recommendations for IHC testing of ER & Pg receptors in **breast cancer**
- ASCO/CAP recommendations for use of HER2 testing in **breast cancer**
- Uses for serum markers of **germ cell tumors**
- Tumor marker tests in the prevention, screening, treatment, and surveillance of **gastrointestinal cancers**
- KRAS gene mutation testing in patients with **metastatic colorectal carcinoma**
- Epidermal growth factor receptor (EGFR) mutation testing for patients with **advanced non–small-cell lung cancer**
- Prostate-specific antigen testing in the screening of men for **prostate cancer**

ASCO Biomarker Guidelines
Focus on Clinical Utility

- RCTs are gold standard for evaluating clinical utility of a biomarker (A)
- Retrospective studies using archived samples from large prospective RCTs offer acceptable strategy (B)
  - eg, cetuximab and WT *KRAS*
- Most marker studies, ie, prospective (C) or retrospective (D) observational studies of convenience of very limited to no use for addressing clinical utility

Analytical Validity	**Ability of the test to yield consistent results**
Clinical Validity	**Ability to predict outcome**
Clinical Utility	**Effect on outcomes, eg LE, AEs, quality of life**
Economic Validity	**Cost benefit and cost effectiveness**



Simon RM, Paik S, Hayes DF: JNCI 2009; 101: 1446-52
Altman DG, Lyman GH: Br Ca Res Treat 2008; 52: 289-303

Biomarkers to Guide Decisions on Systemic Therapy for ESBC
ASCO Guideline Objectives and Perspective

- Identify biomarkers have demonstrated clinical utility to:
  (A) guide decision on need for adjuvant systemic therapy, and
  (B) inform choice of specific drugs or regimens
- Evaluate appropriate assays, timing, and frequency of measurement
- Assessment of clinical utility of genome-wide sequencing for mutational status requires a comparison of outcomes of alternative management strategies with vs without marker.
- Prospective RCT ideal but prospective-retrospective studies offer potentially evidence if results are independently confirmed.

Biomarkers to Guide Decisions on Systemic Therapy for ESBC
Literature Search Results

- PubMed and Cochrane Library searches through Jan 04, 2014
  - 2024 publications identified across the biomarkers considered
- 38 potential studies with “GWAS” or “sequencing” in any field
- Only two studies addressed clinical utility of mutations found by sequencing or related methods.
- Presented results indicated prognostic value (clinical validity) but no evidence of clinical utility.
- Most GWAS and NGS studies in search primarily focused on mutations that alter cancer susceptibility

ASCO Quality and Value Initiatives

ASCO GUIDELINES™

QOPI® THE QUALITY ONCOLOGY PRACTICE INITIATIVE

ASCO CANCER LINQ™
Learning Intelligence Network for Quality

Choosing Wisely®
An initiative of the ABIM Foundation

American Society of Clinical Oncology
ASCO®
American Society of Clinical Oncology
Five Things Physicians and Patients Should Question

Value in Cancer Care Task Force

ASCO GUIDELINES™
Clinical Tools and Resources

QOPI® The Quality Oncology Practice Initiative

900 Participating Practices
167 Certified Practices

PRACTICE AREAS
Staffing
Treatment Planning & Chart Documentation
Informed Consent
Chemotherapy Orders
Drug Preparation
Chemotherapy Administration
Patient Monitoring and Assessment
Preparedness for emergency situations
Oral Chemotherapy
Patient Education

ASCO GUIDELINES
Clinical Tools and Resources

ASCO CancerLinQ: The vision

- Compile and analyze information in real time on patient characteristics, including comorbidities, treatment, clinical outcomes, side effects with tumor molecular profiles if available

- Help prioritize RCTs to test hypotheses most likely to improve care based on predicted magnitude of benefit and size of affected population

ASCO Roundtable on Consensus Standards for Multiplex Cancer Genomic Testing: April, 2014

- Sponsored by ASCO, the Association for Molecular Pathology (AMP) and the College of American Pathologists (CAP)
- **Goal**: Define best approach to ensure cancer patients & specialists have access to high quality genomic testing and easily understood test results for Clinical Decision-Making
- **Objectives**:
  - Develop stakeholder consensus on standards to address clinical validity of multiplex cancer genomic testing and interpretation
  - Discuss evidence base necessary to evaluate the clinical utility of tests and how to generate evidence efficiently
  - Discuss evidence necessary to help insurers determine for whom and when reimbursement of multiplex genomic tests is appropriate
  - Identify challenges and opportunities to promote collaboration of pathologists and oncologists in a clinical management team
  - Recommend standards for test results and reporting that integrates molecular and surgical pathology data