Challenges in capturing long-term outcomes: A view from NCI

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Overview

- Link to Sara Dodson’s presentation
- Questions
  - Examples of some approaches in pilot/feasibility type projects
  - Strengths & limitations of approaches
- Challenges
- Potential future directions
- Collaborators
Investment by NIH & Others

- Identification of public health need and scientific opportunity
- Research initiatives
- Funding acknowledgments
- Funding amount (when feasible)

Research-to-Practice Milestones → Timeline

- Publications (basic to applied)
- Patents
- Industry licenses and development activities
- FDA approvals
- Clinical practice guidelines and recommendations
- Evidence of hand-off to other actors in the medical and public health spheres

Organized by Stream of Impact

- Health
- Knowledge
- Society
Questions

- Tracing the chain of evidence & gathering diverse types of evidence:
  - How can we measure longer term outcomes or impact of NCI-funded research?
    - More specific examples:
      - What is the role of NCI support in:
        - expert-identified scientific advances?
        - breast cancer biomarkers?
        - FDA-approved drugs?
        - guidelines for treatment, screening & detection, and supportive care?
  - Attribution – describing the roles of all players:
    - How does NCI/NIH-sponsored research fit within the larger context of national and global cancer/biomedical research?
<table>
<thead>
<tr>
<th>Question</th>
<th>Key Data Products</th>
<th>Basis</th>
<th>Linkages to NCI funding may be established via:</th>
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<tbody>
<tr>
<td>What is the role of NCI support in <strong>expert-identified scientific advances?</strong>?</td>
<td>“Major” and “notable” advances from <em>Journal of Clinical Oncology</em> (JCO) (2005-2012)</td>
<td>Journal articles, conference presentations</td>
<td><img src="true" alt="Funding Ack." /> <img src="true" alt="Author Affiliation" /> <img src="false" alt="Ack. of Gov’t Interest" /> <img src="false" alt="Clinical Trial Sponsor" /></td>
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<td>What is the role of NCI support in breast cancer <strong>biomarkers</strong>?</td>
<td>Breast cancer biomarkers curated by scientists and integrated into the <em>Thomson Reuters Integrity databases</em></td>
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<td>What is the role of NCI support in <strong>FDA-approved drugs</strong>?</td>
<td>FDA-approved drugs indexed in <em>FDA Orange Book</em></td>
<td>Journal articles (non-patent references)</td>
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<td>What is the role of NCI support in <strong>guidelines</strong> for treatment, screening &amp; detection, and supportive care?</td>
<td>Guidelines published by <em>National Comprehensive Cancer Network (NCCN)</em> in 2012</td>
<td>Journal articles</td>
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What is the role of NCI support in expert-identified scientific advances?

- **Source:** Journal of Clinical Oncology (JCO) Clinical Cancer Advances Series
- **Key data:** Expert panel-identified “major advances” and “notable research” from JCO “Clinical Cancer Advances” series (2005-2012)
- **Basis:** cited journal articles, conference presentations, FDA press releases and underlying clinical trials
- **Linkage to NCI:** funding acknowledgements, intramural author affiliations, clinical trial sponsors
JCO Clinical Cancer Advances

Source

Journal Article

- Collect and analyze acknowledgements; check list of authors for NCI intramural

Presentation

- Get presentation/watch video
- Analyze acknowledgments; Check list of authors for NCI intramural
- Find underlying trial(s) in clinicaltrials.gov,

FDA Press Release

- Analyze acknowledgments/authors in journal articles reporting results of trials

List of acknowledgements/authors

Non-NCI acknowledgement

NCI acknowledgement

Standardize name of funder; classify funder type

Extract award number, NCI activity code
Strengths & Limitations - JCO Analysis

- **Strengths**
  - Advances identified by expert panel
  - Updated annually for most recent calendar year; includes recent conference presentations

- **Limitations**
  - Analysis considers only *JCO*-cited publications
  - Expert panel membership changes over time, may influence identification of advances
  - Publications may not acknowledge all sources of support
  - If multiple sources of support listed, not feasible to determine relative contribution of each
What is the role of NCI support in breast cancer biomarkers?

- **Source:** Biomarkers Module of Thomson Reuters Integrity℠ – a manually curated database of biomarkers with standardized terminology classifying biomarkers into lifecycle phases and disciplines
- **Key data:** Piloted with breast cancer biomarkers in the Biomarkers Module of Thomson Reuters Integrity databases
- **Basis:** specific PubMed journal articles mentioning biomarker
- **Linkage to NCI:** funding acknowledgements
Biomarkers

Biomarker

Indication

Use

Validity

References

PMID

NCI Funding

Thomson Reuters ScienceWire Publication Catalog

Thomson Integrity Manually-Curated Databases

Population

Role (e.g., prognosis, diagnosis)

Technique

Substrate (e.g., plasma, tissue)

Early/Late Stage

Breast Cancer

Literature references used as links to NCI funding
Strengths & Limitations - Biomarkers Analysis

- **Strengths**
  - Expert manually curated robust categorization (e.g., lifecycle phase; disease; use) allows multiple layers of analysis
  - Automated component enables scanning through large publication datasets
  - Links to supporting documents/evidence (e.g., publications, patents, conferences)

- **Limitations**
  - Additional manual curation needed to identify development process stage at which NIH/NCI-funded research contributed
  - Analysis limited to references appearing in MEDLINE-indexed journals
  - Proprietary data source
What is the role of NCI support in FDA-approved drugs?

- **Source:** Approved Drug Products with Therapeutic Equivalence Evaluations (FDA Orange Book)

- **Key data:** Identifies drug products approved on the basis of safety and effectiveness by the Food and Drug Administration (FDA)

- **Basis:** patents cited in New Drug Applications (NDAs), journal articles included in non-patent references, and patents cited by NDA-associated patents

- **Linkage to NCI:** Notices of Government Interest, Intramural Assignees, funding associated with non-patent references
Patent Analysis – FDA Orange Book

1. Acknowledgement of government support
2. Citation of other patents
3. Citation of non-patent references

- Approved Drug (NDA) (FDA Orange Book)
- Patent Number (USPTO)
- Patent Citation Link (ScienceWire Patent Catalog)
- Publication (MEDLINE)
- NCI Funded Project (IMPAC II)
Strengths & Limitations - FDA Orange Book Patent Analysis

- **Strengths**
  - Covers FDA approved drug products with links to relevant patents
  - Links to NCI/NIH support available via notices of government interest, assignees and non-patent references
  - Automated process provides insight into potential links of basic research to downstream outputs; includes estimation of linkage strength

- **Limitations**
  - Access to standardized data for non-patent references for linkage to Web of Science / MEDLINE; proprietary vs public
  - Strength of linkages: direct links to funding from patent; indirect links via cited patents & non-patent references
  - Additional analysis required to qualify the nature of the contribution of the basic research to drug development process
What is the role of NCI support in guidelines for treatment, screening & detection, and supportive care?

- **Source:** The National Comprehensive Cancer Network® (NCCN®) Guidelines for cancer treatment, screening & detection, and supportive care

- **Key data:** Guidelines developed by topic-specific expert panels

- **Basis:** cited references / publications

- **Linkage to NCI:** If references were journal articles, automated searches of NIH databases (SPIRES, MEDLINE) used to find NIH and NCI award numbers
NCCN Guidelines

Extract references manually from guidelines

Not journal article

No further analysis

Journal article

Query NIH SPIRES database

No NIH acknowledgement

Identify as “non-NIH”

NIH acknowledgement

Non-NCI NIH acknowledgement

Identify as non-NCI IC

NIH acknowledgement

Extract NCI activity code
Strengths & Limitations – Guidelines Analysis

- Strengths
  - Single organization uses experts to develop sets of cancer guidelines with consistent methodology and regular updates
  - Journal article references can be extracted and searched for in existing bibliometric databases
  - Closer proximity to clinical application & health impact

- Limitations
  - Analysis limited to references appearing in peer-reviewed journal articles that are MEDLINE-indexed
  - Counting references may be too simplistic
  - Approach may understate role of NCI intramural funding
  - Reliance on acknowledgments may understate NCI and other NIH IC funding
How does NCI/NIH-sponsored research fit within the larger context of national and global cancer/biomedical research?

- No single comprehensive source covering cancer research funding for:
  - Other federal agencies
  - Not-for profits
  - Industry
  - States
- Available sources:
  - International Cancer Research Partnership (ICRP)
  - Potential future sources: Federal RePORTER, World RePORT
- Past approaches:
Challenges

- **Tracing from funding to societal benefits in full context**
- **Data availability**: public vs proprietary; re-purposing administrative data for impact-related analyses; lack of comprehensive analysis-ready data sources
- **Automated vs manual / machine vs expert-identified**; optimal blend?
- **Directness of links / Proximal vs distal** – how close is close enough?
- **Level of analysis / perspective** – project, program, initiative, institute, NIH, US or global biomedical enterprise
- **Retrospective vs prospective identification of high impact** – can we predict high impact, when?
- **Interpretation** – what does it mean?; is it actionable – can we do anything about it?
Potential Future Directions

- **JCO Advances Analysis**
  - Follow citation chains further to underlying basic research
  - Track advances forward in time for metrics of importance

- **Patent Analysis**
  - Expand to include indirect links to NCI support
  - Case studies of selected drugs

- **Guidelines Analysis**
  - Check overlap of NCI-supported NCCN references with other measures of publication importance
  - Case studies of NCI influence on specific NCCN guidelines
  - Convergence of multiple methods to identify case study candidates
  - Tracing forward to societal benefits (e.g., use in clinical practice)
Collaborators

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