Measuring Investigator Impact in Clinical Oncology with the Continuous Innovation Indicators™

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Thank you to HRA for the invitation

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Key team members and collaborators include:
- Silvia Paddock, Rose Li and Associates
- Maneesh Kumar, Breast Cancer Research Foundation
- Carole Wegner, V Foundation for Cancer Research
Goals

• Better understand one dimension of how grants from two foundations contribute to progress against cancer
• Assess how long it takes for basic research to measurably impact the treatment landscape
• Determine whether differences in long-term impact correlate with grant characteristics
• Use the results to inform strategic grant portfolio management
• Disseminate success stories to showcase impact
PACE Continuous Innovation Indicators (CII)

- Database and interactive tool that records, visualizes, and measures progress against 13 solid tumors
- Free for all to use for non-commercial purposes
- Includes evidence for increased overall survival from clinical trials, observational studies, and meta-analyses
- Shows that progress takes time and critically depends on basic research findings, follow-up studies, evaluation of combination therapies, and refinement of existing approaches

The PACE CII translates this complex, dynamic process into easy-to-understand visuals and quantitative scores. See http://scoringprogress.com
Grant Programs Examined

• V Foundation for Cancer Research (VF)
  • 221 early career investigators funded between 1992-2010
  • Focus on all types of cancer, from basic to translational research

• Breast Cancer Research Foundation (BCRF)
  • 159 established investigators funded between 1992-2011
  • Focus on breast cancer only, from basic to clinical research
Methods – Linking Studies

Identify grantees funded until 2010/11
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Find all publications 5 years before award to present (2017/18)

Export references
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Extract references

Grantees

PACE CII
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First degree match

Identify matches

Diamonds indicate identical studies in the two datasets
Methods – Linking Studies

Identify grantees funded until 2010/11

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First degree match

Second degree match
Methods – Linking Studies

Identify grantees funded until 2010/11

Find all publications 5 years before award to present (2017/18)

Find all publications citing grantee pubs

Extract references

Extract references

Export references

Identify matches

First degree match

Second degree match

Third degree match

Fourth degree match

Diamonds indicate identical studies in the two datasets
Caveats

• We conducted the linkage using novel scripts connecting to the NCBI Entrez E-Utilities (https://www.ncbi.nlm.nih.gov/books/NBK25497/).
• We make no claims that this linkage comprehensive.
• Additional follow-up is necessary before drawing any conclusions about the productivity of individual researchers.
• Our approach cannot be used to make valid comparisons of impact between funding organizations.
V Foundation V Scholar Grants

• 207 early career investigators funded between 1992-2010
• Classified by V Foundation into four categories:
  B = biomarker or genomic signature
  C = cancer biology
  G = general cell biology
  T = treatment-related
• 14 out of 221 scholars excluded due to name disambiguation issues or evidence of abandoned grants.
VF Results: Number of Linkages

Most of the 207 V Scholars in the analysis were classified as C type, followed by G, T, and B.

**But:** The average number of linked publications was largest for the B-type grants, followed by C, T, and G. The differences were highly significant (p<0.01).

B = biomarker or genomic signature
C = cancer biology
G = general cell biology
T = treatment-related
VF Results: Time to Impact

The average time for G grant linkage was 11.2 years, whereas T grant publications were quoted significantly faster (average 7.8 years).

Boxplot: Median, first and third quartile, and total range are shown. $p<0.0001$

B = biomarker or genomic signature
C = cancer biology
G = general cell biology
T = treatment-related
VF Results: Summary

- Number of linked grants and time to impact differed by grant type
  - B and T grants created significantly more and faster impact
- G grants more likely to have longer chains of citations
  - *Investments in basic research require time and iteration before impacting clinical practice*
- G grants had highest percentage of scholars with no connections
  - *Funding basic research may be higher risk*
  - *Even after >11 years on average, we may still not have waiting long enough to see the ultimate impact*
- The distribution of grant types shifted over time
  - Shift from G grants toward more B and T grants over time
BCRF Investigators

- 159 prominent breast cancer researchers funded between 1992-2011
- Classified by BCRF into six major categories:
  1 = biology
  2 = etiology
  3 = prevention
  4 = early detection / prognosis
  5 = treatment
  6 = survivorship
BCRF Results: Number of Linkages

- 142 of 159 investigators (~90%) had at least one linkage
- 28 investigators (~18%) had first degree linkages

Histogram - How many grantees had 50, 100, 150, etc. links?
BCRF Results: Time to Impact

1 - Biology

2 - Etiology

3 - Prevention

4 - Early detection / Prognosis

5 - Treatment

6 - Survivorship
The first 3 categories constitute a group with slower impact compared to the last 3 categories.
BCRF Results: Summary

• We identified linkages for nearly 90% of investigators
• Time to impact differs significantly across grant types
  • Biology, etiology, and prevention grants take longer to impact the clinical literature than early detection / prognosis, treatment, and survivorship grants
• Composition of BCRF portfolio was stable over time (p = 0.92)
• Two grant categories strongly influenced by single grantees
  • Etiology (12 investigators had >50 linkages, 4 had >100)
  • Prevention (4 investigators had >100 linkages, 1 had >800)
Overall Summary Results

• The **pattern of impact by grant type was similar** between the two datasets.
  • *Funders can use these consistent differences as one dimension to construct and manage a portfolio of grants with the desired mix of short/long-term risk/impact.*

• Compared to the VF study, the BCRF dataset generally had more links per scholar. This is likely due to all research being focused on breast cancer, one of the cancers in the CII. The VF scope is much broader and includes cancers not in the CII (e.g., leukemias, childhood cancers).

• The BCRF dataset has a lot more first-level linkages than the VF, because the BCRF funds investigators who focus on clinical trials or those whose work ranges from basic biology to clinical trials.

• Both analyses highlighted many **individual impact stories**.
Example Story – Bench to Bedside

1994  Basic science identifies a new mechanism for treatment resistance
2006  Cell line work on the resistance mechanism shows how it can be reversed
2011  More work in cell lines demonstrates how a specific new treatment can reverse the resistance
2013  Phase II trial shows efficacy of this new treatment
2018  ...ongoing: Phase III trial now running...

Green: Publication from BCRF investigator.

Blue: Evidence from the PACE CII database.

Orange: This story is continuing. Research takes time.
Lessons Learned

• Time horizon for impact
  • 10+ years
  • Varies on portfolio mix
• Collecting data
• Characterizing portfolio
• Communicating success stories
  • Most successes are not quick breakthroughs
  • Finding clear, concise ways to communicate complex and cumulative achievements is a challenge – but it is possible!
<table>
<thead>
<tr>
<th>Challenges</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name disambiguation</td>
<td>Maintain bibliographies from grantees</td>
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<tr>
<td></td>
<td>Middle initials</td>
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<tr>
<td></td>
<td>Curated commercial databases</td>
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<tr>
<td>Categorizing grants in portfolio</td>
<td>Consider portfolio goals</td>
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<tr>
<td></td>
<td>Collect with other routine data if possible</td>
</tr>
<tr>
<td>Self-citation; insular citation networks</td>
<td>Read papers to see citations in context; ensure they are meaningful and positive</td>
</tr>
<tr>
<td>Citing reviews instead of primary sources</td>
<td></td>
</tr>
<tr>
<td>Big papers with 400 co-authors</td>
<td>Consider excluding from analysis</td>
</tr>
<tr>
<td>Attribution of impact in case of multiple funders</td>
<td>Challenging. This method is better suited for differences between groups than absolute statements</td>
</tr>
<tr>
<td>Communicating complex success stories</td>
<td>Simplify, but provide context</td>
</tr>
<tr>
<td></td>
<td>Acknowledge interactions with other contributions to realize greater long-term achievements</td>
</tr>
</tbody>
</table>
What do I need to do something like this?

• Some technical coding skills or partnerships
• Data on existing and past grants
• Set of publications representing key achievements
  • Cancer – PACE CII freely available at [http://scoringprogress.com](http://scoringprogress.com)
  • Other disease areas
    • Identify set of seminal papers
    • Fields with no treatments – collect data, categorize, ID goals for each domain, ID pivotal papers in that domain, then work backwards
• Contact us!
  [Samuel.Thomas@roseliassociates.com](mailto:Samuel.Thomas@roseliassociates.com)
NCBI E-Utilities

• Programming interface to NIH databases, including PubMed

• Compatible with any computer language that can send a URL to the E-utilities server and interpret the XML response
  • Examples: Perl, Python, Java, and C++

• https://www.ncbi.nlm.nih.gov/books/NBK25497/

• https://www.youtube.com/watch?v=BCG-M5k-gvE
Identifying Seminal Papers

- Clinical guidelines citations
- Cochrane reviews
- “Advances in [disease of interest] Research”

www.tsalliance.org

Cites 58 key studies

IACC publishes annual list of ~20 top advances in Autism Spectrum Disorder research
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