Finding The Right Metrics For Evaluating Big Science

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  - “Waiting for the moonshot”
- Especially for Big Science programs
- Are mid-term assessments feasible?

RESEARCH-TO-PRACTICE MILESTONES FOR GLEEVEC®

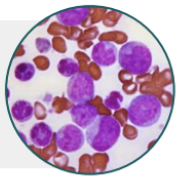
For more information on the supporting evidence and research sponsors for the following milestones, see the Web appendix table.

IDENTIFYING THE MOLECULAR TRIGGER OF CML (1914-1990)

1914 — Biologist Theodor Boveri first had the idea that chromosomal abnormalities might play a role in tumor development, but no tools existed at that time to test his hypothesis.[8]

1950s — New scientific techniques helped researchers link chromosomal abnormalities to specific diseases.[9]

1960 — The altered chromosome in CML cancer cells was discovered and named the "Philadelphia chromosome," after the city in which it was discovered.[10] NIH



1973 — The cause of the abnormal Philadelphia chromosome – a chromosomal translocation – was identified.[11]

1983-1984 — NCI researchers determined that ABL1, a gene that was known to be involved in some cancers, was altered by the chromosomal translocation.[12,13] NIH

1985 — The protein (BCR-ABL) created from the cancer-causing gene was determined to be a protein kinase, a class of cell-signaling molecules. The BCR-ABL protein constantly signals to a cell that it is time to divide, leading to cancer.[14] This finding inspired researchers to look for ways to inhibit BCR-ABL signaling as a treatment for CML. NIH

DEVELOPING A TARGETED BCR-ABL KINASE INHIBITOR (1990-1996)

1990 — NIH-funded researcher Dr. Brian Druker began developing model systems to study BCR-ABL kinase signaling and explore ways to inhibit it.[15] NIH

Scientists at the pharmaceutical company Ciba-Geigy (which later became Novartis) started to refine a compound that blocks the actions of the BCR-ABL kinase.[16]

1992 — Imatinib, the compound that would become Gleevec®, was first created, as part of a larger collection of compounds to test.[17]

1993 — Dr. Druker and his colleagues partnered with Ciba-Geigy to study their collection of compounds for signs of anti-cancer activity.[18] NIH

1996 — Imatinib (Gleevec®) was shown to kill cancerous cells without harming healthy ones by blocking BCR-ABL kinase signaling.[19] NIH

1997 — The Food and Drug Administration Modernization Act[20] allowed the FDA to create a "Fast Track" mechanism that makes important new drugs available to patients more quickly.[21]

TESTING AND APPROVING A LIFE-CHANGING DRUG (1997-2015)

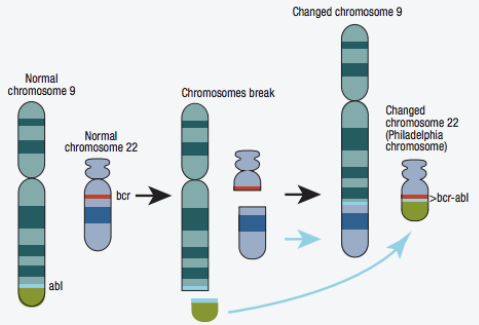
1998 — The pharmaceutical company Ciba-Geigy prepared Gleevec® for use in patients, and the first NIH-funded Phase I clinical trial began. The trial yielded an astounding positive response rate of 98%, as all 31 patients experienced remission with limited side effects.[22] NIH

2001 — FDA granted "Fast Track" designation for Gleevec®, speeding up the review process because Gleevec® treated a serious condition with no known cure. FDA approved it only 10 weeks after the New Drug Application was submitted by Novartis.[23]

2006 — A follow-up clinical study found that after five years of continuous treatment, the vast majority of CML patients receiving Gleevec® remained cancer-free.[24]

NIH *indicates NIH-funded milestones*

SCHEMATIC OF THE PHILADELPHIA CHROMOSOME FORMATION



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- Members of Congress motivated by “electoral connection,” incentive to direct funding to constituents
  - Politics of the pork barrel: bias to majority, institutional power
- Hypotheses:
  - Success at selling science (persuade MCs to keep hands off) contingent on ability to distinguish good science from bad
  - Cross-agency variation in political influence explained by differences in ability to distinguish, not geographic scope of work

What Do Program Directors/Officers Think?

- Consistently supportive of the need to measure longer-term impact and the need to develop a better system for doing so
- …greatest challenge in measuring the impact of funded science?
  - “We have the wrong metrics and the timeline is too long.”
- …considering the impact or “success” of funded projects, do you make distinctions between short-, medium-, and long-term impacts?
  - “Yes. The challenge is that NASA Science is looking at the longer term. Decision makers often are not.”
- …useful to think about assessing the impact of research at different stages of development?
  - “Yes, but right now decisions are made based on informed opinion rather than data”

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- Second task: understand how an approach will influence the grant-making process
  - Characterize incentive to game the assessment process

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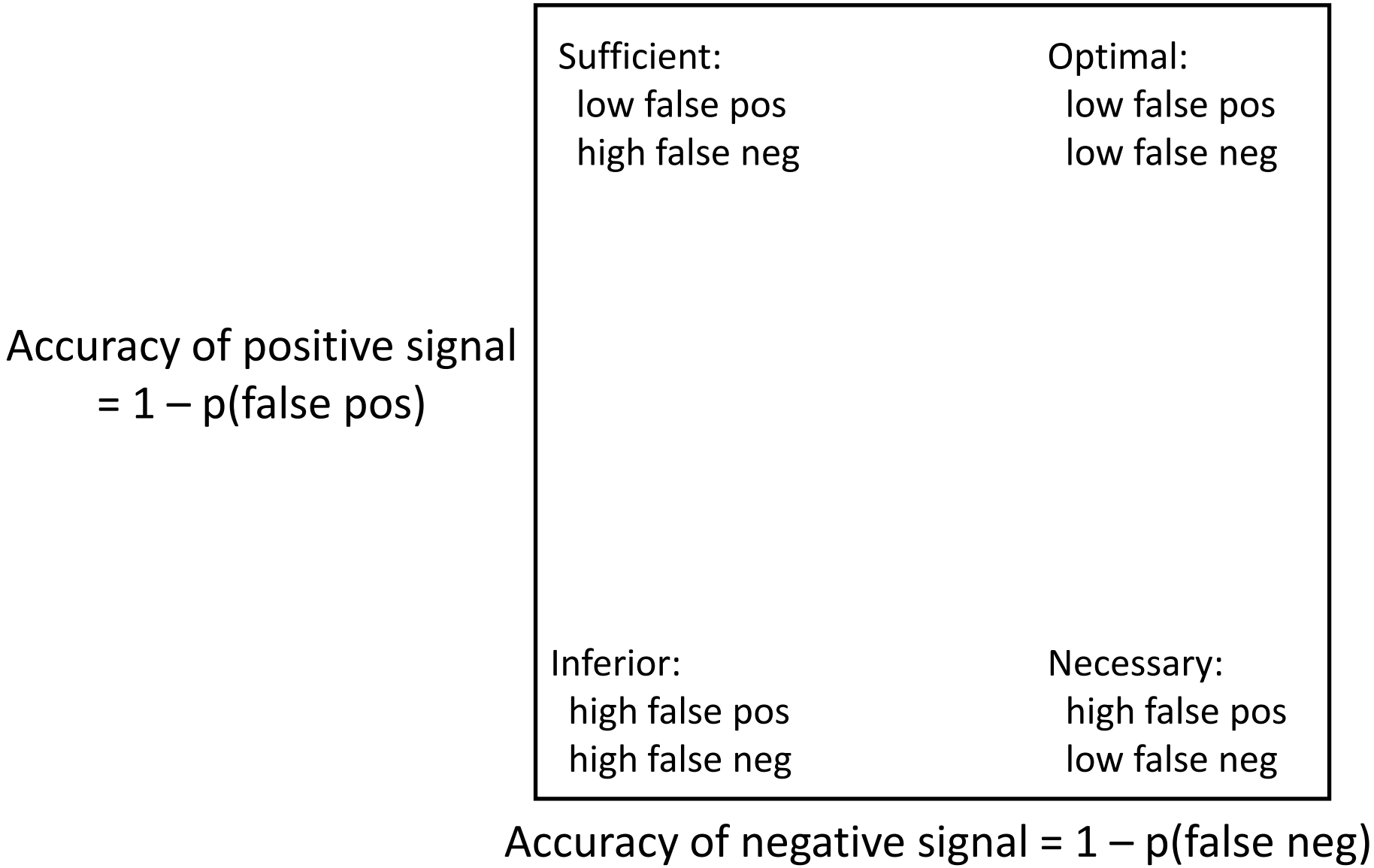
- Solve for outcomes using Perfect Bayesian Equilibrium

Types of Waypoints



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- Waypoint characteristics (diagnosticity, false pos, false neg)
- Impact of waypoint pursuit on innovation rate
- Attractiveness of alternate projects (base rate)

Preliminary Findings

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- Usefulness of waypoints depends on context:
  - When alternative project is attractive, prefer sufficient waypoints
  - When alternative unattractive, prefer necessary waypoints

Empirics: Commercialization of ISS Research

- Commercialization Endpoint: defined as entry into commerce of an ISS-related innovation for a non-space, non-NASA market (14 out of 318)
- Candidate waypoints: Patents, Citations, Publications in high-impact outlets
  - Conditioning Factor: Sector of PIs (corporate vs. academic)
- NASA-funded project must play a significant role in origin of the innovation (not mere testing of an off-the-shelf product)

Fun With Data

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- Non-linear innovation pathways
  - KES Science’s AiroCide® ethylene-mold removal system
- Key contributions by small and medium enterprises (SMEs)
  - AMS enabled by small entities such as Space Cryomagnetics Ltd.

Results from Multivariate Logistic Regression

>100 "Good" Cites	Corporate PI: Patent	Corporate PI: No Patent	No Corporate PI: Patent	No Corporate PI: No Patent
Yes	-	0.496	-	0.178
No	0.253	0.003	0.07	0.001

Next Steps

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  - Impact of second-order effects: availability of alternates
- Expand:
  - Additional waypoints: follow-on funding (SBIR, etc.)
  - Full accounting for game-ability of waypoints
  - Particularly for ISS program, PI incentives to reach endpoint
  - Add endpoints: scientific discovery, engineering research

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  - Contrast with NASA's attempts to justify ISS
- Accept that some programs cannot be protected from political influence without additional work
  - Vital role for peer review process
- Innovation as incremental process rather than one-and-done