Why and How NCI Uses Cooperative Agreements: U01 Focus

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Purpose of analyses

In spring 2020, BSA and NCAB requested information on why and how NCI uses cooperative agreements, specifically U01s.

In response, we conducted qualitative and quantitative analyses of U01 programs, awards, and their purpose and outcomes.

Overview of NCI U01s

- Policy definitions of cooperative agreements
- NCI's reasons for using U01s
- NCI U01 awards from FY10 to FY19, comparisons with R01 awards
- Conclusions, discussion

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Cooperative agreement definition and examples

- Cooperative agreements are used when ***substantial programmatic involvement*** is anticipated between the Federal agency and the recipient during performance of the assisted activity.

- NCI examples of commonly used activity codes*
  - U01 *(research project)*
  - U54 *(specialized center)*
  - UM1 *(complex structure)*
  - U24 *(resource-related, project)*
  - U2C *(resource-related, multi-component)*
  - UG1 *(clinical research, project)*
  - U10 *(clinical research, multi-project)*
  - UG3 & UH2 / UH3 *(exploratory, Phase I / Phase II)*
  - UE5 *(education project)*

From NIH policy manual & grants.nih.gov: policymanual.nih.gov/manage/chapter/view/54815, grants.nih.gov/grants/funding/ac_search_results.htm

*NCI examples of programs using these activity codes in appendix

Substantial involvement definitions and process

"Substantial involvement" means that the recipient can expect Federal programmatic collaboration or participation in managing the award.

- NIH purpose is to support and/or stimulate the recipient's activity; *partner role*
- Dominant role and prime responsibility for the activity reside with the awardee(s) for the project as a whole
- IC staff responsibilities are detailed in the Terms & Conditions (T&C) of Award
- T&Cs are customized for individual planned scientific activities
- An IC official must concur on use of the cooperative agreement mechanism

From NIH policy manual: policymanual.nih.gov/manage/chapter/view/54815

How does a cooperative agreement differ from a grant, U01 versus R01 focus?

Activity	R01	U01
Research project	✓	✓
Investigator-led	✓	✓
Funded from RPG	✓	✓
Awardees participate in meetings	✓	✓
NCI involvement	Normal stewardship	Substantial involvement

Range of NCI substantial involvement

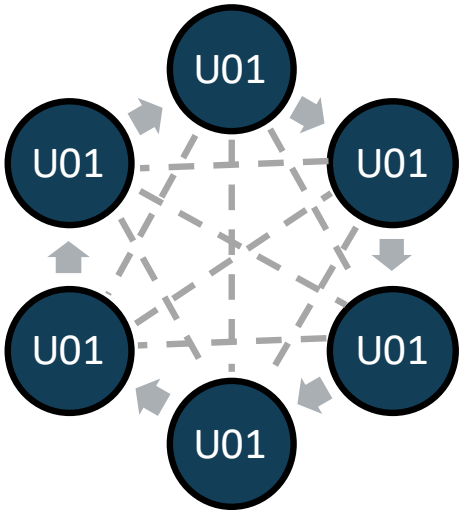
R01 grant management ← **U01 management** → **NCI scientific direction**

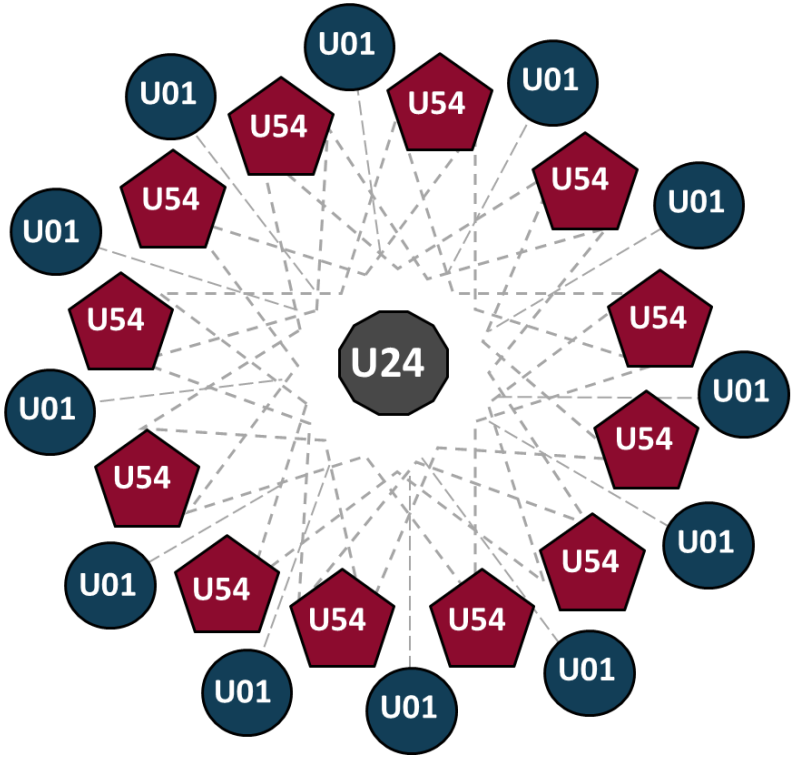
- Coordination of program meetings, collaborative project opportunities

- Network coordination to communicate overall program progress
- Steering committee coordination/ participation for cross-network and trans-consortia collaborative projects

- Network coordination to drive collaborative program goals
- Significant scientific input in project activities
- Facilitating pilot or collaborative projects for specific scientific needs requested by NCI/external partners

Range of complexities of program structures with U01s





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The NCI uses the U01 to *more effectively* facilitate progress toward a shared research goal

- Build a field/discipline/community of practice
  - NCI engagement to support developing research area
  - NCI facilitation of communication across disciplines

- Support collaborative effort on well-defined research need
  - FOA-defined
  - Steering by NCI

- Leverage unique or limited resource
  - Data, biospecimens

Investigator-led projects in U01 programs are enhanced by cooperative agreement activities

Components flexibly added for each program:

- Working groups on areas of interest/importance
- Steering committee
- Collaborative / discretionary / rapid response funding
  - Flexible with some spent at PI's discretion and some controlled by steering committee/NCI
  - Funding almost uniformly for collaborative efforts
- Administrative supplements for inter-network collaboration

U01 programs enable outputs beyond what is possible with an R mechanism

- Enhance coordination and data/resource sharing
- Facilitate tools and approach interoperability, enhance adoption
- Develop resources – biospecimens, harmonized data and operating procedures
- Flexibility to shift to time-sensitive, priority projects, public-health emergencies
- Assure quality control and maximize NCI investment – clinical trials, phases of a large-scale project

Simulation modeling to extend evidence provided by trial, epidemiologic, and surveillance data to guide public health research and priorities

(*consortium of U01s)*

The CISNET U01 enables:

- ***NCI-facilitated, high-impact, public health projects***
  - Analyzed COVID-related delays in the screening and diagnosis of colorectal and breast cancer on excess cancer deaths – 2020 *Science* editorial
  - Assisted with US Preventive Services Task Force screening guidelines for colorectal, breast, lung, and cervical cancers
- ***Emerging opportunities using rapid response funds***
  - Advised CDC's Advisory Committee on Immunization Practices on extending HPV vaccination age indication to 45
  - Worked with Down Syndrome associations to determine benefits/harms of mammography
- ***Consortium-identified, cross-cancer site collaborations***
  - Impact of delays in diagnostic testing after abnormal screen (breast, cervical, colorectal cancer)
  - Personalizing age of cancer screening cessation based on comorbid conditions (colorectal, prostate, breast cancer)

Addressing multiscale and dynamic cancer processes using experiment + computation

(U01 projects as part of a larger consortium)

The CSBC U01 enables:

- ***Field building – expanding community and supporting early-stage investigators***
  - Encourages new, interdisciplinary teams to break into cancer research, encourages new multi-PI research programs on a smaller (non-Center) scale
  - 20% of CSBC U01 contact PIs are ESIs, 35% of MPI teams contain an ESI member
- ***Flexibility – expanding scope of research areas within a larger consortium***
  - Addition of emerging high-priority focus areas that complement U54 Centers research themes, such as tumor and microenvironment co-evolution, stromal and immune communication networks, and the contribution of metabolic crosstalk to drug resistance
- ***Consortium-identified collaborations applying complementary approaches***
  - Overcoming resistance to MAPK inhibition in breast cancer *(3 U01s formed collaboration)*
  - Contribution of rare cell states to melanoma progression and therapy resistance *(U01 + U54 combined technology, computational approaches after discovering similar phenomenon)*

Developing and testing new molecular and imaging biomarkers to detect early stage pancreatic ductal adenocarcinoma and its precursor lesions (*consortium of U01s*)

The PCDC U01 enables:

- ***Unique resource development using harmonized protocols and restricted funds***
  - Pancreatic Cancer High-Risk Family Cohort (N = 2209) - longitudinal collection of biospecimens and data from individuals and family members at risk
  - Pancreatic Cyst Cohort (N = 2215) - longitudinal collection of biospecimens and data from patients with pancreatic cysts
- ***NCI-facilitated collaborations across consortia, NIH awardees, external partners***
  - Alliance of Pancreatic Cancer Consortia (APaCC) – platform/resources to discover and validate biomarkers and imaging methods for early detection *(4 NCI consortia, 2 external partners, other investigators)*
  - APaCC project - multi-institutional imaging repository for pre-diagnostic and early pancreatic cancer cases with clinical annotation
- ***Inter-consortia resource sharing – data, data models, analytical methods, etc.***
  - Infrastructure developed by Early Detection Research Network data coordinating center and NASA's Jet Propulsion Laboratory

The NCI uses the U01 for intramural-extramural collaborations *(individual projects)*

- Access to intramural technologies
  - *e.g., Clinical Center technology, electromagnetic navigation technique for sampling hepatic lesions*
- Access to intramural expertise
  - *e.g., Neurofibromatosis type 1 (NF1) therapeutic expertise, clinical trials*
- Investigation of shared scientific interests
  - *e.g., Prostate-specific membrane antigen (PSMA)-targeted imaging for prostate cancer*

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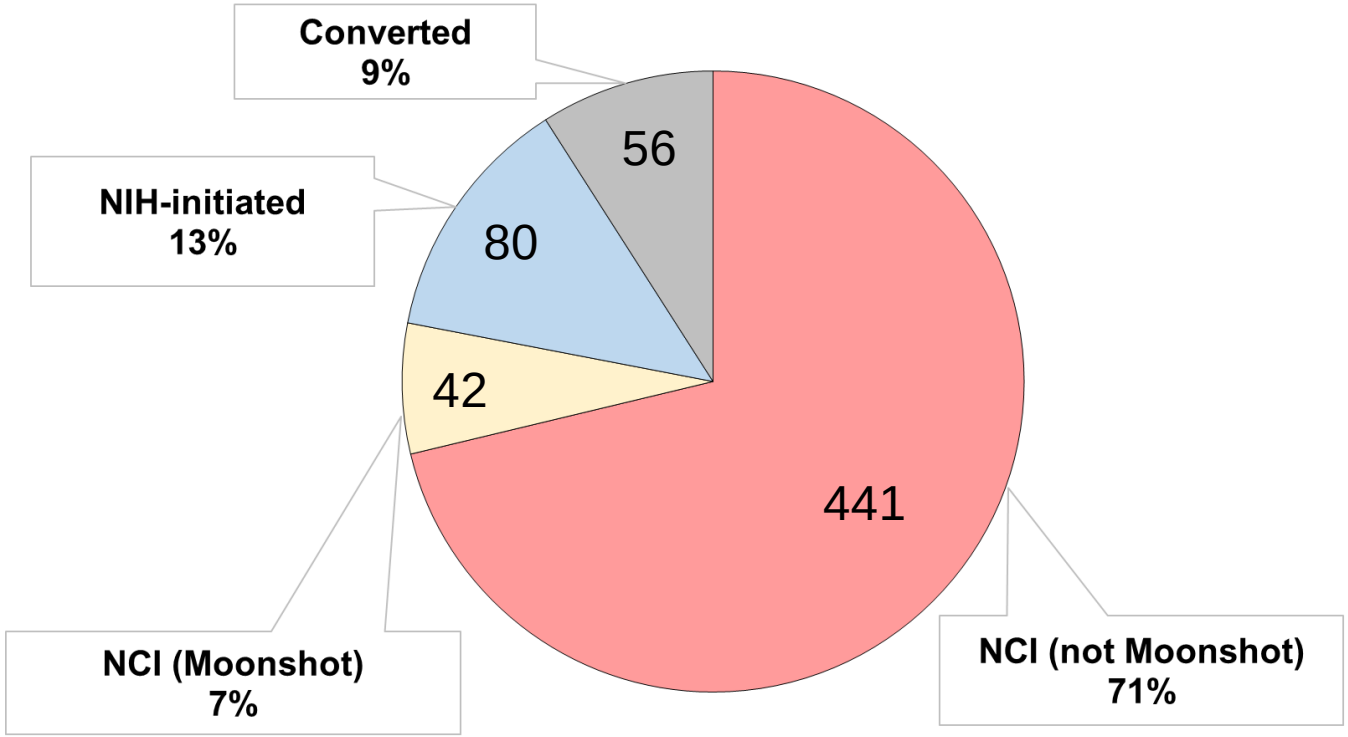
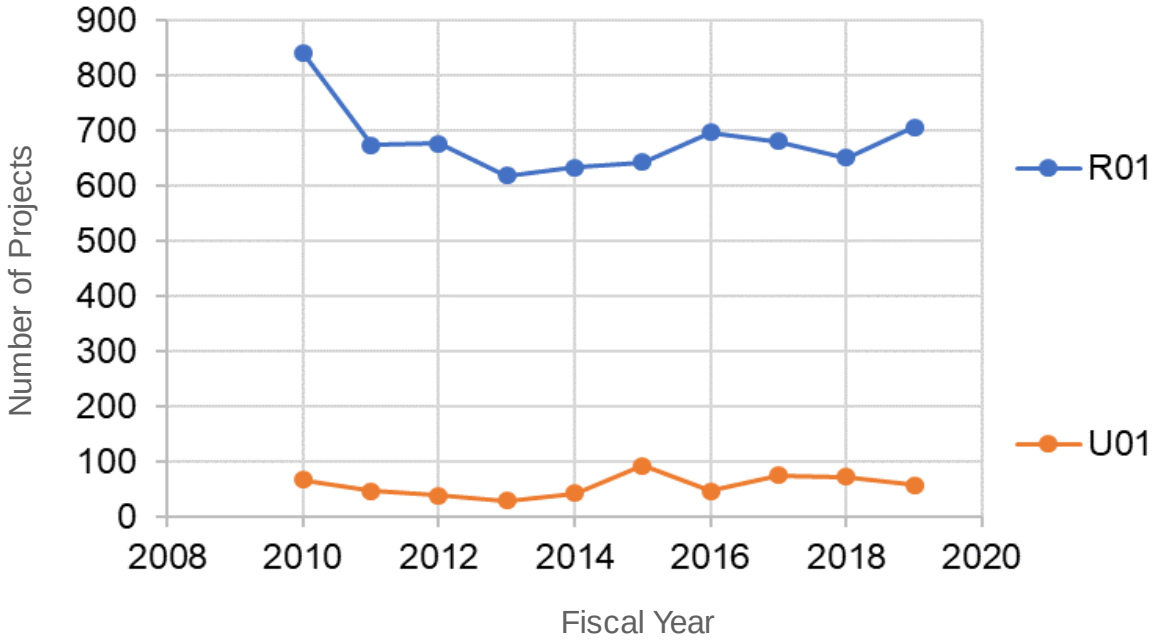
NCI U01 competing projects FY10 to FY19



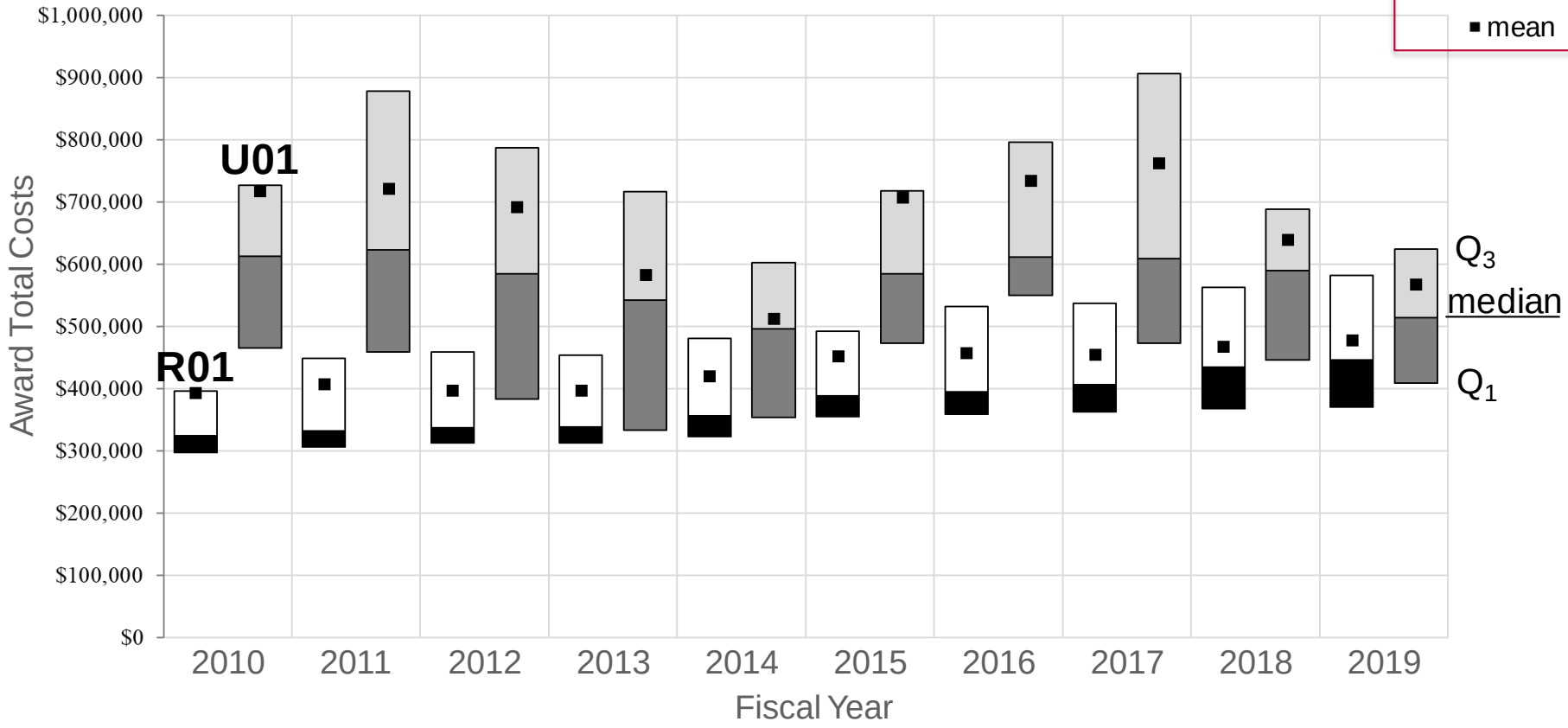
The projects funded through NCI-initiated FOAs represent 60 unique programs.

NCI competing U01 versus R01 projects, FY10 to FY19



Most U01 projects are to NCI- or NIH-initiated FOAs, while the majority of R01 projects are to the parent R01.

Project costs: comparing competing R01s and U01s (excludes Moonshot)



U01 versus R01 key points: FY10 to FY19

Total Projects:

- U01: ~ 60 competing/year [Range: ~30-90]
- R01: ~700 competing/year [Range: ~600-850]

- >90% U01s from NCI- or NIH-initiated FOAs

Total Costs:

- U01: median of ~$600k total cost/year
- R01: median grew steadily from $325k to $450k total cost/year

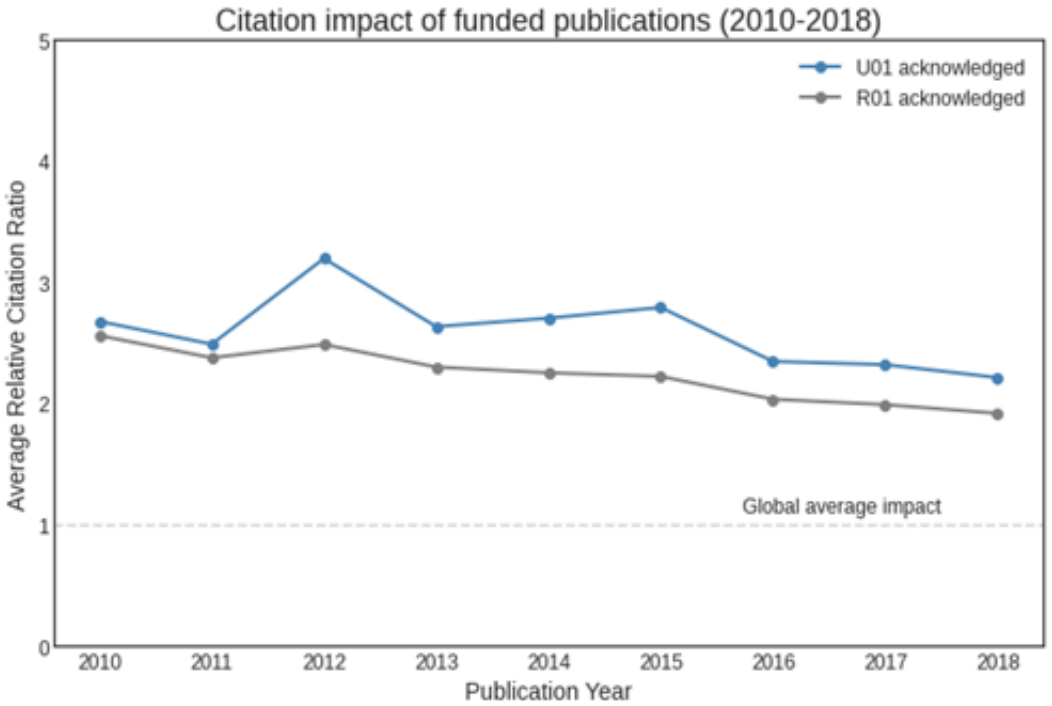
- U01/R01 cost difference due to factors such as: fewer modular awards, more MPI awards, collaborative funds, program infrastructure costs, type of research

Comparing publication outputs of U01s versus R01s

Analysis caveats:

- U01s yield a large variety of output and outcomes (expanded fields/disciplines, collaborations, research resources, etc.)
- As a first look, focused on publications to give a sense of the differences between U01s and R01s

NCI U01s have a slightly larger average citation impact (RCR) compared to R01s



Note: Does not correct for different funding levels

Source: Dimensions for NIH, Digital Science. Includes publications that acknowledge base projects with a competing award between FY 2010 and 2019.

U01s have a slight increase in publication productivity compared to R01s, when correcting for funding levels

Method:

- Compared NCI-funded projects: FY03 – FY12
- Inputs included ***project properties*** (such as funding), ***institution properties*** (such as location), and ***prior achievements of the PI.***
- ***Important Caveat:*** did not correct for all differences between U01 and R01 such as research topic

Key Findings:

Statistical modeling indicated that ***U01s slightly increase*** *(compared to the R01):*

- **the number of publications: *+ 1-3 pubs/project***
- **the citation impact of resulting publications: *+6% average bibliometric percentile/project***

Reminder: This analysis only looks at one small part of output and outcomes

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Cooperative agreement conclusions

- ***Cooperative agreements play an important role in NCI's research portfolio***
- ***Selection should be guided by the scientific needs of an initiative***

- U01s are a small fraction of the NCI RPG pool *(<10% total projects & funding)*, primarily awarded through NCI-initiated funding opportunities

- Effective approach to achieve common goals and enable research outputs that may be more difficult to achieve through R mechanisms
  - Substantial NCI involvement to facilitate and guide activities
  - More efficient research, collaborations, resource development, flexibility

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Matthew Young (DCP)
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Group discussion, questions?

Follow up questions, more data/information:

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www.cancer.gov

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