ACD High-Risk, High-Reward: Working Group Interim Recommendations

ACD Meeting
December 13, 2018

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High-Risk, High-Reward – Unique Common Fund Programs

- Investigator-initiated scientific goals
- Enable investigators to launch a potentially transformative project without preliminary data
  - Risk involved is mitigated by emphasizing past accomplishments during review and by allowing changes of course during the funding period
- Individual awards are 5 years
- Piloting novel application and review processes
High-Risk, High-Reward – Unique Common Fund Programs

Funding opportunities for outstanding scientists at all career stages

The High-Risk, High-Reward Research program supports exceptionally creative scientists pursuing highly innovative research with the potential for broad impact in biomedical or behavioral science. The program’s four constituent NIH Director’s awards provide a diverse set of funding opportunities.
Charge to the Working Group

- Review effectiveness of NIH HRHR research programs
- Analyze participation of women and other underrepresented groups in the applicant, finalist, and awardee pools of HRHR grants to identify possible causes for their underrepresentation
- Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools
- Propose steps that NIH might take to enhance the diversity of applicants and awardees in HRHR programs, while supporting the best science
Review effectiveness of NIH HRHR research programs

• Compared research outcomes of the 33 Pioneers in first 3 cohorts to similarly qualified R01 investigators, random R01 sets, and HHMI investigators

• Assessed scientific impact and innovation through bibliometrics and expert analysis

• Found Pioneer-funded research has
  • More impact than similar and random R01s and about as much impact as HHMI
  • More innovative than similarly qualified R01 investigators’ research and similar to HHMI
Review effectiveness of NIH HRHR research programs

New Innovator Award Outcomes Evaluation Report by the Science & Technology Policy Institute

Table 1. Comparison of bibliometric indicators

<table>
<thead>
<tr>
<th>Bibliometric indicator</th>
<th>NI Awardees compared with ESI R01 Awardees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Citations per Publication</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>IPP (Journal impact factor)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>RCR (Relative Citation Ratio)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>SNIP (Journal Source-Normalized Impact per Paper)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>SJR (Scimago Journal Rank)</td>
<td>NI awardees &gt; ESI R01</td>
</tr>
<tr>
<td>H – Index</td>
<td>No statistically significant difference</td>
</tr>
<tr>
<td>Number of publications</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
<tr>
<td>Average annual publications</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
<tr>
<td>Time to first publication (Faster is greater)</td>
<td>ESI R01 awardees &gt; NI awardees</td>
</tr>
</tbody>
</table>

Evaluated outcomes of NI awardees in first 3 cohorts

- NI-funded research is more innovative, risky, and has more impact than ESI R01 research
- Awards did not have significantly more positive or negative impact on the careers of its awardees than did ESI R01s (risk of research project did not put careers at risk)
Clinical and technological impact: HRHR vs. NIH R01 awards

Type 1 HRHR and NIH R01 awards, FY2011-FY2016

<table>
<thead>
<tr>
<th>Award Type</th>
<th>Number of awards</th>
<th>Awards with clinical impact</th>
<th>Awards with technological impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transformative</td>
<td>76</td>
<td>25 (32.9%)</td>
<td>35 (46.1%*)</td>
</tr>
<tr>
<td>Pioneer</td>
<td>70</td>
<td>17 (24.3%)</td>
<td>20 (28.6%*)</td>
</tr>
<tr>
<td>Independence</td>
<td>88</td>
<td>25 (28.4%)</td>
<td>15 (17.0%)</td>
</tr>
<tr>
<td>Innovator</td>
<td>280</td>
<td>58 (20.7%*)</td>
<td>58 (20.7%)</td>
</tr>
<tr>
<td>NIH R01s</td>
<td>22,559</td>
<td>7708 (34.2%)</td>
<td>3617 (16.0%)</td>
</tr>
</tbody>
</table>

* Statistically significant difference relative to NIH R01s p<0.01
Analyze participation of women and other underrepresented groups … to identify possible causes for their underrepresentation

- Pioneer: no significant difference across review process
- EIA: Significant decrease across review process
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- **Transformative Research award**
  - Cohort Year: 2009-2018
  - Applicants, Finalists, Awardees
  - TRA: variation from year to year, overall no significant increase or decrease

- **New Innovator Award**
  - Cohort Year: 2007-2018
  - Applicants, Finalists, Awardees
  - New innovator: increase is significant from applicant to awardee
Analyze participation of women and other underrepresented groups ... to identify possible causes for their underrepresentation

- The group concluded that, in general, applications from females and URMs are not being adversely affected by the review process
  - For EIA, the percentage of female applicants was higher than awardees until 2018
  - Across all awards, there is year-to-year variation in percentage of applicants who choose not to identify their gender, ethnicity, and race

- Issue and concern: number of applications from women and URMs applying is low
Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools

HRHR applications and awards map to a narrow range of topics that vary widely in award rates

- For all HRHR programs combined, these 21 clusters (14.2% of the total of 148 clusters) account for over half of the applications
- The range of award rates for these clusters is 1.77% to 14.63%
  - Mean award rate = 6.83%
  - Median cluster award rate = 5.21%

<table>
<thead>
<tr>
<th>Topic</th>
<th>Awards</th>
<th>Apps</th>
<th>% of all awards</th>
<th>% of all apps</th>
<th>Award rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model Organisms and Genetics</td>
<td>24</td>
<td>164</td>
<td>4.67%</td>
<td>2.18%</td>
<td>14.63%</td>
</tr>
<tr>
<td>Neuronal Circuits</td>
<td>26</td>
<td>182</td>
<td>5.06%</td>
<td>2.42%</td>
<td>14.29%</td>
</tr>
<tr>
<td>RNA Transcription</td>
<td>12</td>
<td>100</td>
<td>2.33%</td>
<td>1.33%</td>
<td>12.00%</td>
</tr>
<tr>
<td>Gene Regulation</td>
<td>29</td>
<td>250</td>
<td>5.64%</td>
<td>3.33%</td>
<td>11.60%</td>
</tr>
<tr>
<td>Antibiotic Resistance</td>
<td>12</td>
<td>111</td>
<td>2.33%</td>
<td>1.48%</td>
<td>10.81%</td>
</tr>
<tr>
<td>Protein Crystallography</td>
<td>19</td>
<td>192</td>
<td>3.70%</td>
<td>2.55%</td>
<td>9.90%</td>
</tr>
<tr>
<td>Gut Microbiome</td>
<td>11</td>
<td>119</td>
<td>2.14%</td>
<td>1.58%</td>
<td>9.24%</td>
</tr>
<tr>
<td>Systems Biology</td>
<td>25</td>
<td>304</td>
<td>4.86%</td>
<td>4.04%</td>
<td>8.22%</td>
</tr>
<tr>
<td>T-Cell Immunotherapy</td>
<td>7</td>
<td>90</td>
<td>1.36%</td>
<td>1.20%</td>
<td>7.78%</td>
</tr>
<tr>
<td>Tissue Scaffolding &amp; Engineering</td>
<td>17</td>
<td>229</td>
<td>2.92%</td>
<td>3.05%</td>
<td>7.42%</td>
</tr>
<tr>
<td>Stem Cells</td>
<td>15</td>
<td>229</td>
<td>3.31%</td>
<td>3.05%</td>
<td>6.55%</td>
</tr>
<tr>
<td>High-throughput Screening</td>
<td>20</td>
<td>306</td>
<td>3.89%</td>
<td>4.07%</td>
<td>6.54%</td>
</tr>
<tr>
<td>Imaging Methodology</td>
<td>15</td>
<td>240</td>
<td>2.92%</td>
<td>3.19%</td>
<td>6.25%</td>
</tr>
<tr>
<td>Statistics and Modeling</td>
<td>5</td>
<td>96</td>
<td>0.97%</td>
<td>1.28%</td>
<td>5.21%</td>
</tr>
<tr>
<td>GWAS Studies</td>
<td>14</td>
<td>270</td>
<td>2.72%</td>
<td>3.59%</td>
<td>5.19%</td>
</tr>
<tr>
<td>Drug Discovery</td>
<td>6</td>
<td>148</td>
<td>1.17%</td>
<td>1.97%</td>
<td>4.05%</td>
</tr>
<tr>
<td>Software Development</td>
<td>6</td>
<td>148</td>
<td>1.17%</td>
<td>1.97%</td>
<td>4.05%</td>
</tr>
<tr>
<td>Brain Cancer</td>
<td>6</td>
<td>185</td>
<td>1.17%</td>
<td>2.46%</td>
<td>3.24%</td>
</tr>
<tr>
<td>Nanoparticle Drug Delivery</td>
<td>5</td>
<td>178</td>
<td>0.97%</td>
<td>2.37%</td>
<td>2.81%</td>
</tr>
<tr>
<td>Clinical Outcomes</td>
<td>4</td>
<td>156</td>
<td>0.78%</td>
<td>2.08%</td>
<td>2.56%</td>
</tr>
<tr>
<td>Clinical Practice</td>
<td>2</td>
<td>113</td>
<td>0.39%</td>
<td>1.50%</td>
<td>1.77%</td>
</tr>
</tbody>
</table>
Examine institutional diversity and diversity of scientific topics in the applicant and awardee pools

HRHR awards appear bias toward institutions and organizations with large, well-known biomedical research programs.....

The Office of Portfolio Analysis looked at:
- Award distribution and rates using descriptive analysis and multivariate regression
- Productivity trends

**Bottom line conclusions:**
- Overall, the quality of work resulting from awards directed to institutions and organizations with smaller research programs and ”top-tier” institutions was not significantly different
- Similar productivity and quality
Interim Recommendations

OUTCOMES

The working group agrees there is value in having HRHR programs and that the awards have greater influence on certain scientific areas as compared to traditional R01s.

- Overall successful program, expand if possible
- Formally evaluate the Transformative Research Award
Interim Recommendations

OUTREACH

The HRHR working group recognizes that encouraging women and underrepresented minorities to apply for HRHR awards is of critical importance to increase their representation among the awardees.

- Initiate a special HRHR program that requires a collaboration between an under-resourced institution and resourced institution and addresses diversity in the broadest sense
- Build a career development portal that centralizes all NIH training grants and efforts
  - [https://researchtraining.nih.gov/](https://researchtraining.nih.gov/)
  - [https://researchtraining.nih.gov/programs/other-training-related](https://researchtraining.nih.gov/programs/other-training-related)
- NIH should host workshops where institutions can send 1-2 students to learn about all training opportunities
Interim Recommendations

OUTREACH

- Provide on the HRHR website prototype example grants similar to the template examples available for R01s and K awards
- Certain HRHR application features can be applied to other NIH grants to enhance broader success of underserved groups
  - New Innovator features should be applied to a special award type for Early Stage Investigators (ESIs)
Interim Recommendations

BIAS

The group acknowledges that there appears to be bias in the topics that are awarded under HRHR programs. Clinical studies tend to be underrepresented, as do other behavioral, psychological, and sociological topics.

- Special track or separate HRHR program for clinical outcomes; separate review track
- In FOAs for all the HRHR awards, reiterate that all topics are welcome; underrepresented topics can be emphasized
- Continue to ensure reviewer expertise in topics underrepresented in award topic maps and matching of reviewer expertise to applications
Interim Recommendations

BIAS

HRHR awardees primarily represent a subset of the top-tier research institutions.

Options:

- Elevate institutional diversity as a program priority
- Cap the number of applications each institution can submit
- Cap the number of applications each institution can submit, but factor in size of institutions and scale the permissible number of submissions accordingly
Interim Recommendations

BIAS

Average representation of females and underrepresented minorities in the applicant pool is reflected in the awardee pool, but there is fluctuation from year to year and the numbers in many cases are small. The group agrees potential for unconscious bias should be mitigated.

- Reviewer education or training
- For the Pioneer and Early Independence awards, move approach review to first phase and keep only biosketch for the final review
Interim Recommendations

HARASSMENT

- Require HRHR grantee organizations to provide assurances that they have effective, fair, and up-to-date policies to preserve a harassment-free environment
- If HRHR grantee institutions become aware of harassment findings related to HRHR grantees, they should alert and work with NIH to arbitrate the situation
Timeline

- After evaluating and analyzing the HRHR programs, propose steps that NIH might take to enhance the diversity of applicants and awardees in these programs, while supporting the best science
  - Final recommendations: June 2019 ACD meeting
NIH...
Turning Discovery Into Health