

Transitioning your Pilot Award or K-Award to an R01

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or... How to Write a Successful
R01 the first time!

Outline

- NIH K Awards
- My perspective
- Early Stage Investigators
- The Research Question
- Scoring Criteria (With a focus on preparing your R01)
- Timing

NIH Career Development Award Program

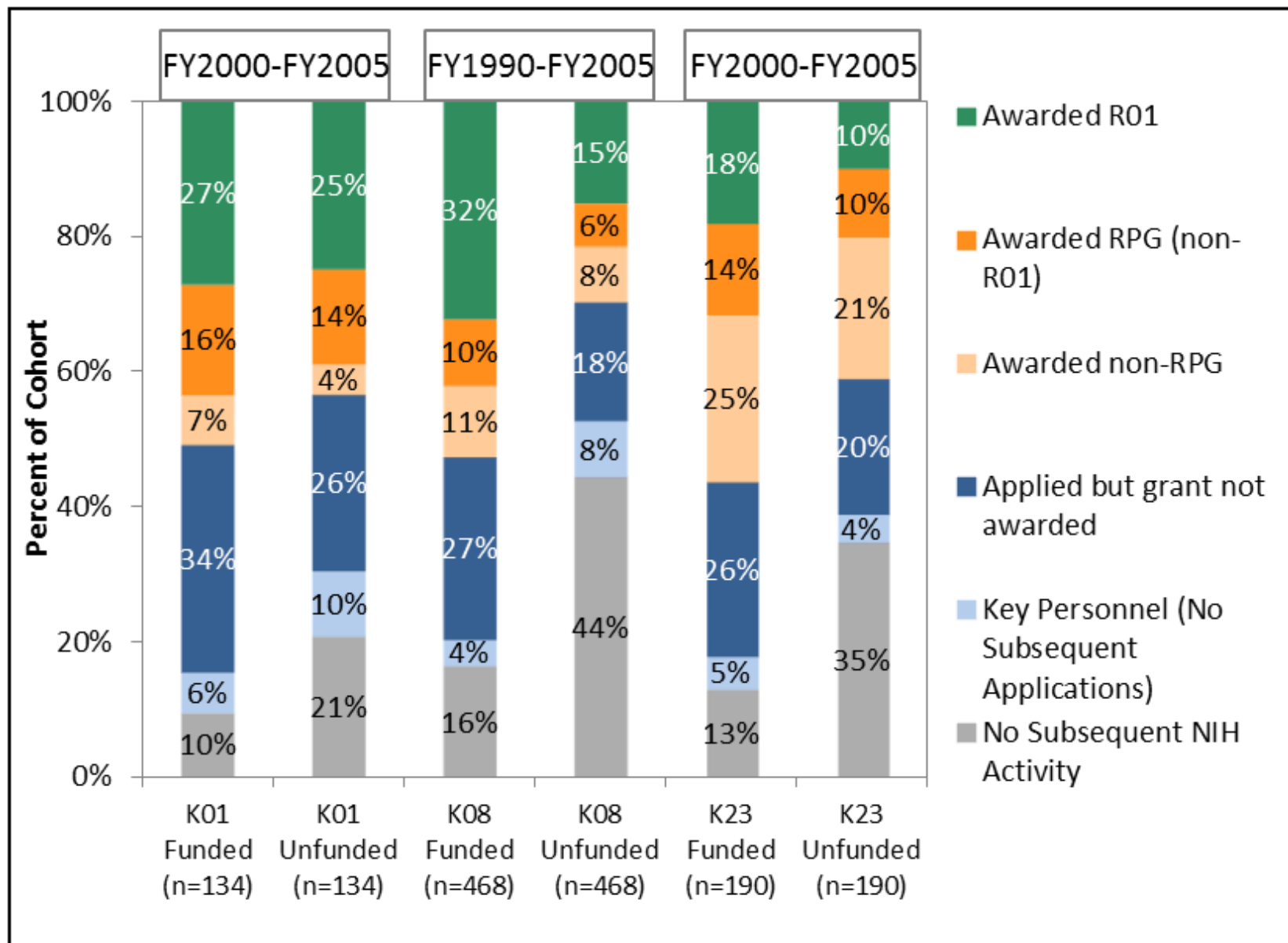
- The objective of the NIH Career Development Award program (K award) is to provide salary and research support for a sustained period of “protected time” (3-5 years) to ensure a future cadre of well-trained scientists who will become competitive for NIH research project (R01) grant support.

NIH K Awards

- **K01 – Mentored Research Scientist Development Award (Ph.D.)- usually basic research**
- **K08 – Mentored Clinical Scientist Development Award (M.D. or other clinical degree)- usually basic research**
- **K23 – Mentored Patient-oriented Research Career Development Award (M.D. or other clinical degree)**
- **K99/R00 – Pathway to Independence (PI) Awards**
- **K22- Transition Award- 2-3 years at NIH; 2-3 years at extramural academic institution in U.S.**
- **K24 – Mid-Career Investigator Award in Patient-oriented Research (M.D.)**

Subsequent NIH grant outcomes, by K program

Source: NIH Extramural Nexus, Sept 2011



Are K awards fulfilling their purpose?

- Overall, the answer is yes. Looking at comparable unfunded and funded applicants, those who received a career development award were more likely to:
 - remain in research,
 - publish in scientific or medical journals,
 - apply for an NIH research grant,
 - receive an R01, and, for those who could be followed long enough,
 - apply for and receive a renewal.

*A randomized study
would have been a
better approach!*

Elements of K awards that support R01

- Research experience
 - Preliminary data collection
 - Collaboration with mentoring team
 - Operational experience (IRB, cores, staff)
 - Publications and presentations
- Training
 - New expertise
 - New collaborators



My Perspective

- Standing member of KNOD Study Section (Kidney Nutrition Obesity Diabetes)
- Focus on patient-oriented research
- Mentor for three faculty with successful transitions:
 - K01 to R01
 - R21 to R01
 - WFSM intramural funding to R01
 - In each case, the pilot award was a ‘mini-version’ of the R01
- Mentor for two faculty with transition plans:
 - K12 (& R21) to R01
 - Foundation (AHA) to R01

NIH: Special consideration for Early Stage Investigator (ESI)

- *ESI = within 10 years of completing their terminal research degree or medical residency at the time they apply for R01 grants*
- Peer reviewers will focus more on the investigator's experience and training rather than the record of accomplishments that have advanced the investigator's chosen field.
- Peer reviewers do not expect ESIs to provide the same depth of preliminary data as they expect from an established investigator.
- ESIs will receive 'bonus points' in funding decision (i.e., funded at a higher percentile) and may undergo an expedited review on a revision.
 - e.g., NHLBI FY11 payline is 16% for non-ESI (A0) and 26% for ESI
 - NIDDK: 15%, 17%

The Research Question

- The overarching question that your research intends to examine.
- Must pass the 'so what?' test.
- *A natural extension of your pilot work.*



Scoring Criteria

- Significance
- Innovation
- Investigators
- Approach
- Environment



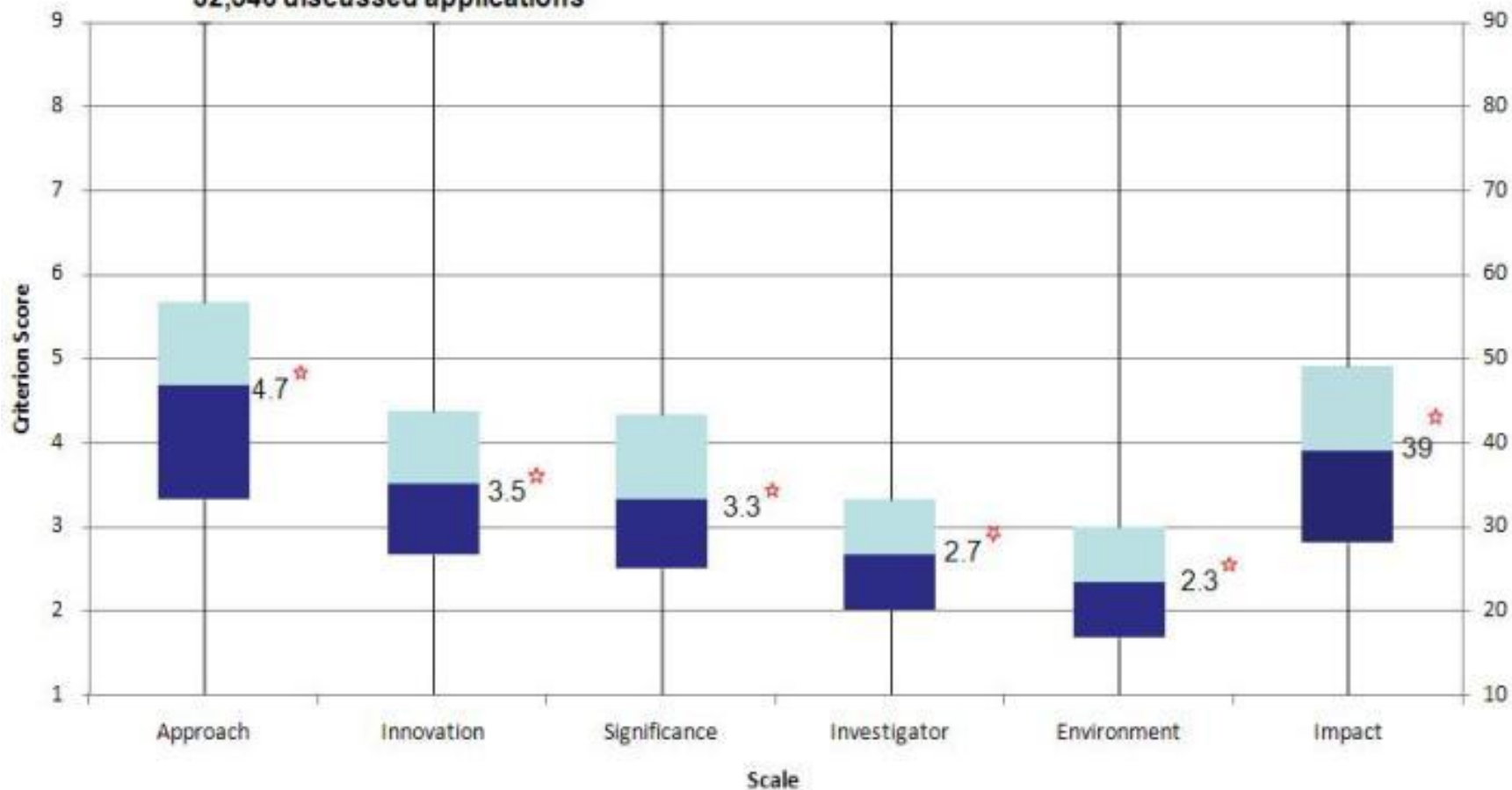
Summary Score: Overall Impact

- The likelihood (based on the approach, investigators and environment) that the work will exert a sustained powerful influence (based on significance and innovation) on the field.
- The bar is clearly 'higher' for an R01 than for a pilot or K award!

Distribution of Criterion Scores

FY 2010: October, January, May Councils
54,727 submitted applications
32,546 discussed applications

☆ Median score



Multiple Regression Model Predicting Impact Scores using Criterion Scores

Criterion	Regression Weight
Approach	6.7
Significance	3.3
Innovation	1.4
Investigator	1.3
Environment	-0.1

Investigators

- You as the Early Stage Investigator
 - Usual elements: training, experience, publications, grants
 - Highlight your ‘training’ from your K award period
- Collaborators/co-I
- Consultants



Collaborators

- Retain as many of your original (pilot study) collaborators as possible (and reasonable)
 - “Choose your pilot study collaborators carefully”!
- For ESI applications, reviewers often look for previous collaborations with your investigators as support of potential future success
- Reviewers are often skeptical of a team that has not previously worked together
- Important to have some published abstracts and/or papers with your collaborators

Publish

- Publish (and/or present) your preliminary results at the earliest possible opportunity
 - National scientific meeting (abstract)
 - Short report in peer-reviewed journal
 - Full length article
- Include as co-authors, collaborators who will be key personnel on R01
- Find other opportunities to collaborate on related research, particularly to participate as co-author to build your CV in this research area



Approach

- Approach drives the IMPACT score!
- The Approach is often described separately for each Specific Aim:
 - Specific Aim/Hypotheses
 - Rationale
 - Preliminary Data
 - Methods
 - Statistical Analysis and Power

Preliminary Data

- Often considered the key reason for the K award or pilot award
- Despite reduced page limitations, a clear presentation of preliminary data are still critical for R01 funding
- Many goals of preliminary data:
 - Feasibility
 - Effect sizes for power calculations
 - Proof of concept
 - Acceptability of an intervention, burden, safety

Preliminary data: Feasibility

- Your experiment (albeit, on a smaller scale), in your hands, at your institution
- Ability to secure resources (e.g., CRU, staff)
- Ability to access stored “freezer” samples
- Ability to recruit, retain participants
- Assess data completeness, reliability of the measures, acceptability to participants

Some Measures of Feasibility

1. Number screened to reach number randomized, yield, time required
2. Percent of data items complete
3. Percent of participants refusing certain study measures (questionnaires, invasive tests)
4. Time required to adjudicate medical records, agreement (kappa) among reviewers, availability and completeness of records (percent)
5. Reliability of laboratory assays (CV)



Preliminary data: for statistical power

- Pilot data are often generated to provide statistics necessary to calculate statistical power, specifically
 - Effect size (e.g., difference in outcome measure between two intervention groups)
 - Variance (standard deviation)

Preliminary data: Proof of concept

- Evidence which establishes that an idea (model, process) results in the anticipated outcome.

Example: (1) Pilot epidemiologic data suggest that a dietary fiber intake is associated with reduced accumulation of abdominal/visceral fat.

(2) Pilot study was designed to investigate whether a dietary supplement of fiber (compared to control) will result in reduced accumulation of abdominal fat.

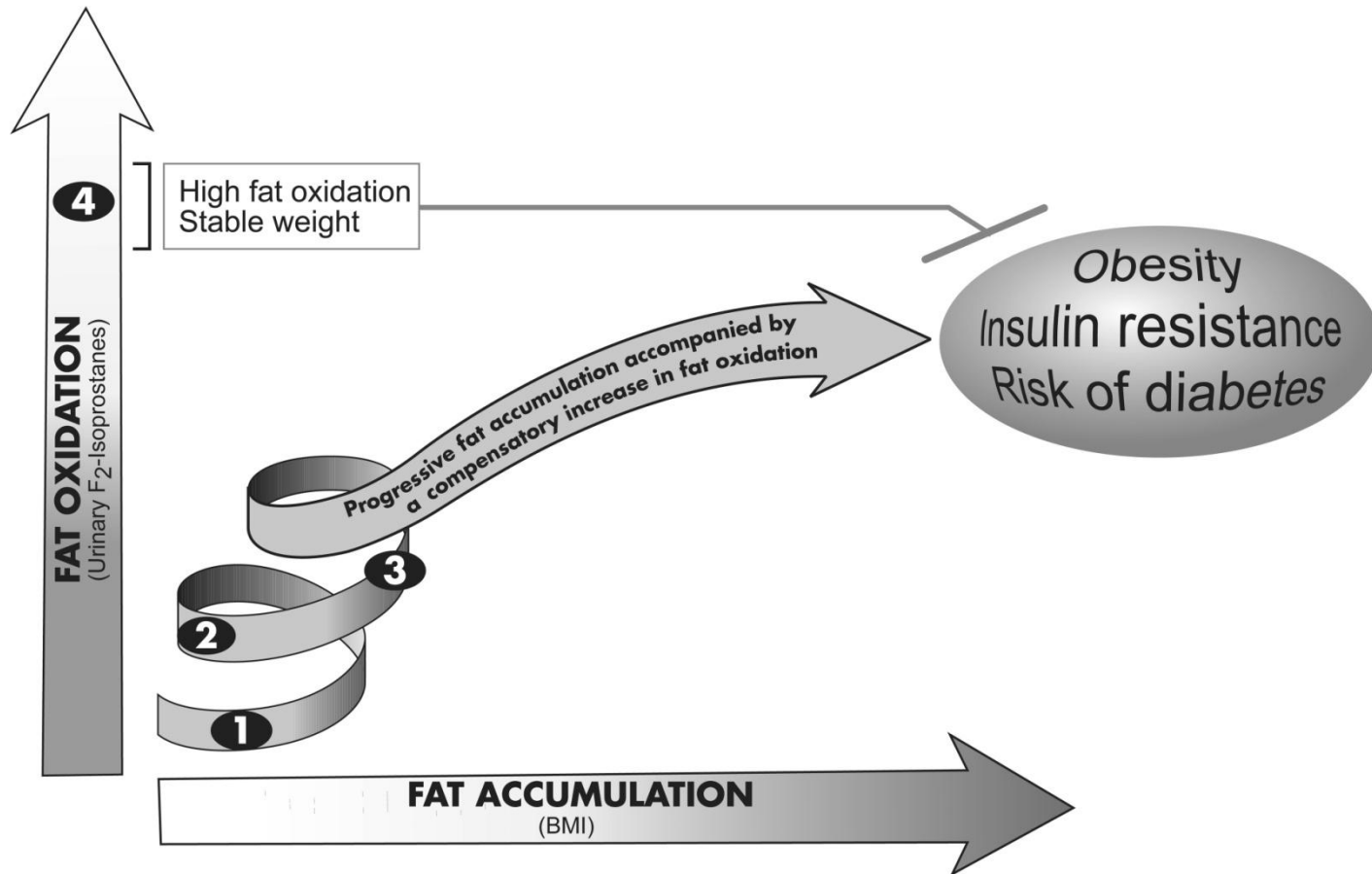
(3) Plan for R01 to test in randomized trial whether dietary intake of fiber will result in reduced accumulation of abdominal fat.

Preliminary data: Acceptability

- Intervention delivery
- Measurements (e.g., invasive)
- Burden (participant and/or staff)
- Evidence of low risk (safety/small N)
- Point out how you have refined your research plan based on the results of your pilot studies.
 - In a recent R01, we wrote a section: “Lessons learned from the pilot study”, indicating changes to the intervention based on feedback from the participants.

What to do if ...?

- Your preliminary results do not support your hypothesis, either null or contrary?
 - **Make the best of it:** power considerations/consider other biologically plausible mechanisms
- You encounter obstacles with recruitment, the intervention, measurement
 - **Make the best of it:** Collect detailed information and use it to adjust your study design (longer intervention; change inclusion/exclusion criteria)
- Your results are conclusive and the R01 is not needed!
 - **Make the best of it:** expand to subgroup effects, other outcomes



- 1** *Poor fat oxidation predisposes to fat accumulation*
- 2** *Larger fat storage leads to an adaptive increase in fat oxidation. Fat oxidation is higher, but not enough to compensate for positive energy balance.*
- 3** *Sustained positive energy balance leads to further increase in fat storage, obesity, and increased risk of insulin resistance and diabetes.*
- 4** *Strong individual ability to oxidize fat prevents the development of obesity, thereby reducing the risk of diabetes.*

Environment

- Generally, institutional resources as they support your grant
 - Facilities (how have you accessed these in your pilot study?)
 - Collaborative environment
 - Support for new investigators, mentoring
 - Unique resources (TSI, Design & Analysis Unit)



When do you submit the R01?

- BEFORE the pilot award ends!
- Issues to balance:
 - Completeness of preliminary results: partial results are often OK (depends on the depth of other support for your research question).
 - Your personal funding situation.
 - Only one revision allowed. Thus, it must be excellent the first time in; revision can incorporate more pilot data.
- I prefer an earlier submission, even in the absence of definitive preliminary results.

