

The application: significance, preliminary data, and approach

Hulley – chapter 19

GW Workbook – chapters 9,10,11

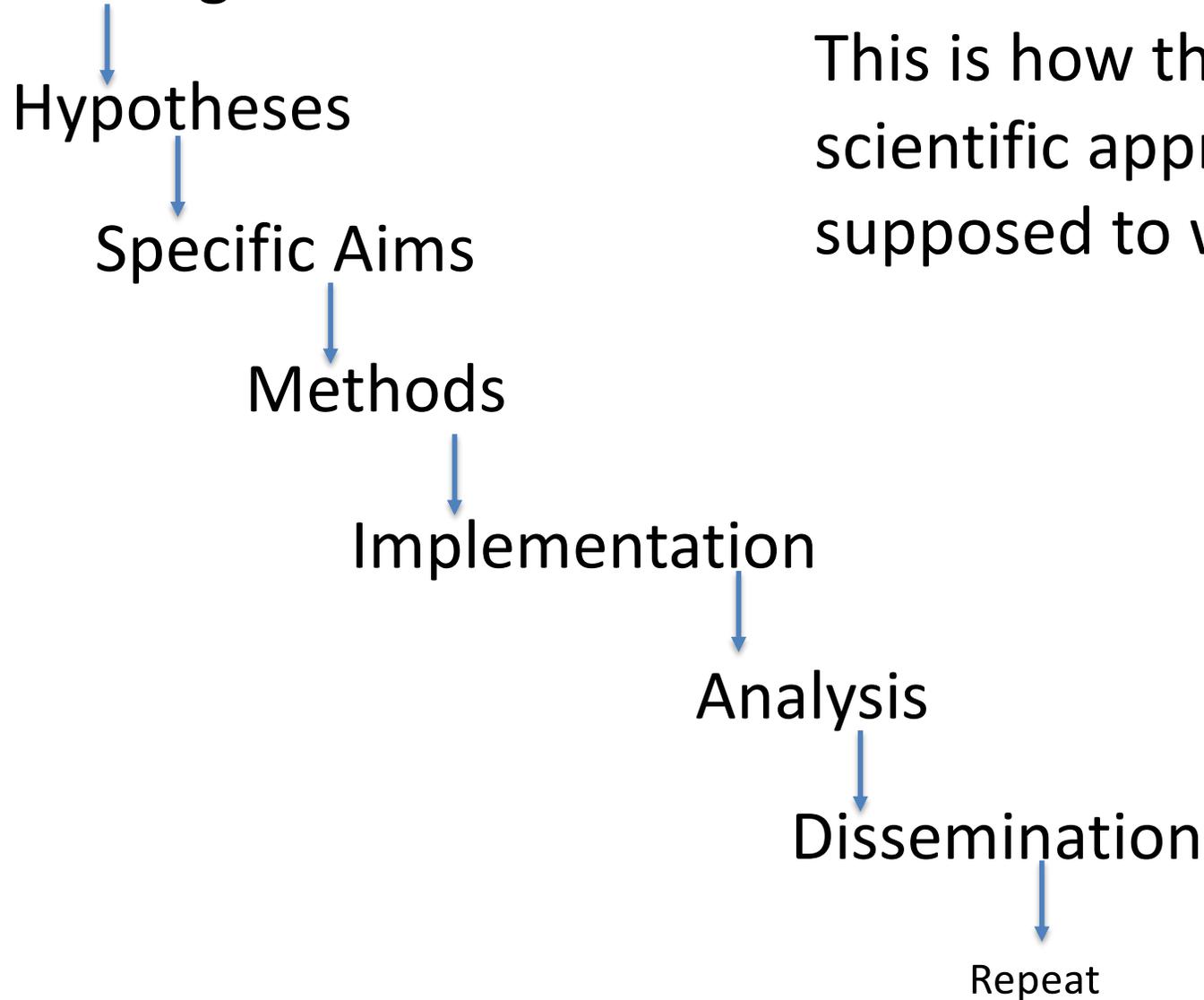
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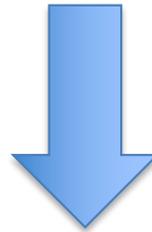
Background & Significance



Review Guidelines

- Significance / Relevance
 - Is the problem important? How will science be improved?
- Investigators
 - Do investigators have appropriate experience and training to conduct research?
- Innovation
 - Does project shift current clinical practice paradigms?
- Approach
 - Are methods well-reasoned, unbiased, feasible?
- Environment
 - Are resources available to conduct project?

Will my research get funded?



Scoring Domains

Significance	Innovation	Investigators	Approach	Environment
Preliminary Data				
Impact				<u>Unscored</u>
				Ethics
				Budget

You must not be impartial. You must be the strongest advocate for your proposal.

It is the right study at this time to address this important problem.

Significance Section

- Write a condensed story that introduces reviewers to the research
- First 2-3 pages, or a brief overview with detailed write-up for each specific aim
- Provides a rationale for why you have developed your hypotheses and specific aims.

Significance - comments

What is the basis for your research ('so what'?)

- What is the problem
- What do we know now
- Quickly move the text to your hypothesis
- Highlight the part of the problem you are attacking
- Show your preliminary results addressing gaps

Significance – other comments

- You are trying to build desire for your study - **Do not be boring**
- What is the big picture
 - Facts, theoretical framework
 - Lit review can not be comprehensive. **Get to the point.**
 - Go deep only into the **most relevant research**: seminal studies and recent studies defining state of knowledge
- Rigor of existing science
 - **Highlight** problems and gaps
 - Show your judgement in the presence of uncertainty
- Impact
 - Research contribution upon completion
 - Simple statements of credible positive impacts to the field
 - Relevance to NIH

Significance – additional comments

- Can be treated as a ‘test’ for the PI
 - Cite your publications whenever you can.
 - Provide new preliminary data
 - Demonstrate your expertise

You are telling a story...

Your Process

- read...write....repeat
- Continuously re-evaluate your hypothesis and aims
- Search other fields for innovation to apply
- Find others with preliminary data that compliments your PD

- Have others read it, and acknowledge their comments
 - Content experts / mentors / peers
 - Professional writers / proof-readers
 - Educated but no content expertise

How a reviewer sees Significance

- Do I care about this question/Impact/so what
 - Why do I not understand it?
 - Is it well written?
- Do other reviewers care about this question?
- Are preliminary data compelling?
- How does it translate to the research study?

- Other scoring criteria are focused on study implementation and feasibility

Preliminary Data

- PD is almost always required, and if not required, is usually expected.
- Significance:
 - Establishes the foundation for each hypothesis and specific aim
 - “These are interesting results, and we should study this further.”
 - Clarity of data presentation is critical.
 - Includes tables, figures, or graphs. Use footnotes extensively, and map descriptive text to figures and tables.
 - Make sure your PD strongly supports your hypothesis
- Approach
 - Demonstrate feasibility or superiority of your data collection protocols
 - Repeat previously published approaches with references
 - PD may come from any member of the research team
- **The quality of the preliminary data is scored!**
 - Reviewers will look at PD carefully.
 - It should be a sample of what you think the final results might look like.
 - Do not include PD if it is of poor quality, distracting, or not relevant

Innovation

- NIH is less interested in 'me too' research
- Depart from the status quo.
 - Use a new theory, method, approach, or intervention
 - Then explain how novel aspects increase study significance
 - Innovative hypothesis or question
 - Sometimes a strange idea is an innovative idea
- Usually one paragraph, and re-stated throughout application
- Define the status quo in the literature
- State your innovation and how it improves your project

Approach

- Describe the overall strategy, methods, and analysis for each aim
 - What will be done
 - How will you do it
 - Who will do it (if not obvious)
 - What are the expected outcomes
 - What might go wrong
 - What are alternative approaches
- This may be the easiest section to write because you have already conducted pilot work and developed research protocols.

Approach (for each aim)

- Introduction (1 paragraph)
 - overview /objective / hypothesis
 - statement of the rationale, approach, impact
- Research Design
 - Describe each study activity
 - Justify model systems
 - Power and sample size
 - Statistical methods
 - Preliminary feasibility data / publication quality
 - Reference published methods / common protocols /standards
 - Rigor
 - Expected outcomes (1-2 paragraphs)
 - Problems (make sure they are minor)
 - Alternatives (1 paragraph)
 - Timeline for all aims and benchmarks (make a table or figure)
 - Future directions / what is the next step

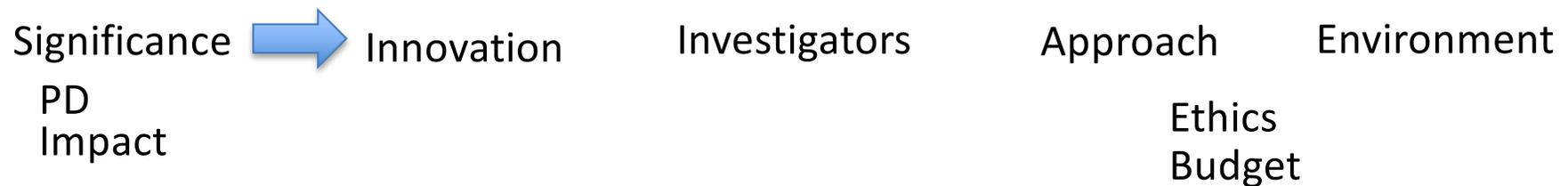
Approach

- 8-10 pages
- Try to use equal space for each specific aim
- Simplify descriptions as much as possible
- But, include enough detail in the most critical areas
- Data analysis. Do not forget the statistical analysis – get adult biostatistical support
- Advocate for the study by demonstrating expertise, feasibility, innovation, and impact

Other sections

- Investigators
 - Biosketches
 - One paragraph describing team interactions
- Environment
 - Facilities section
- Not scored, but discussed
 - Budget
 - Human Subjects / Animal protection

Will my research get funded?



Of the scored domains, Significance is sine qua non. Without significance, nothing else matters.

If found significant, Approach is usually most criticized. Reviewers often want more clarity and detail. They do not care about page limits.

Try to highlight all innovation in one place. Don't expect reviewers to know what is innovative about your proposal.