

Data science thinking: making an impact

Kostas Sechidis & Mark Baillie
AMLD, Lausanne
March 24th, 2024



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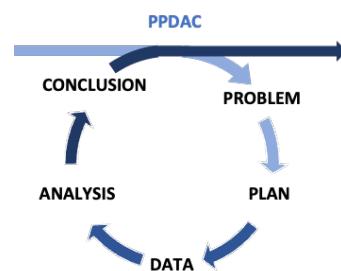
Today's agenda

Schedule

- 35 mins
- 55 mins
- 30 mins
- 55 mins
- 30 mins

Activity and topics

- Introduction:** motivating data science thinking
- Problem & Plan:** getting questions right
- Break
- Data & Analysis:** developing & executing a strategy
- Conclusions:** effective visual communication



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All the materials and
more are online

<https://datascience-thinking.github.io>



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Who we are ...

Mark Baillie



Kostas Sechidis



Prashanti Goswami



Frank Bretz



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Getting to know you!

What's your background:
academia, industry, public
sector, or other?

Do you consider yourself a
data scientist?

What do you hope to learn
from this workshop?

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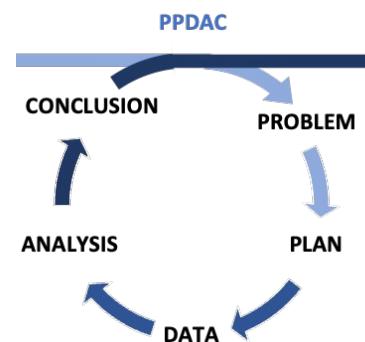
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Data science thinking process

A set of integrated **thinking skills** and practices
refocused for answering questions with data

A good **workflow** is an established set of habits that
help drive you forward towards your goal. They enable
complexity to scale in the right areas.

This workflow demonstrates the steps for abstracting
and solving **a real problem**. An impactful solution
requires a clear understanding of how things work.



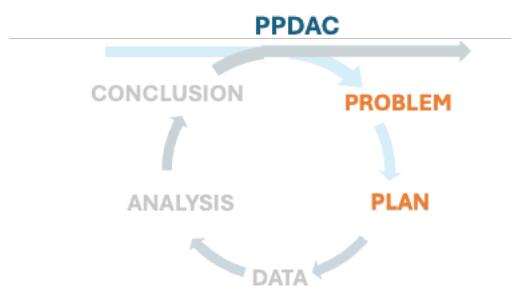
Source: MacKay, R.J. and Oldford, R.W., 2000. Scientific method, statistical method
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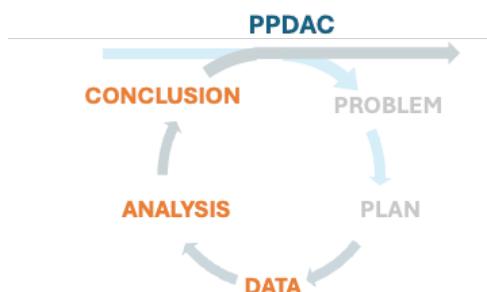
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Data science thinking: making an impact

Part I



Part II



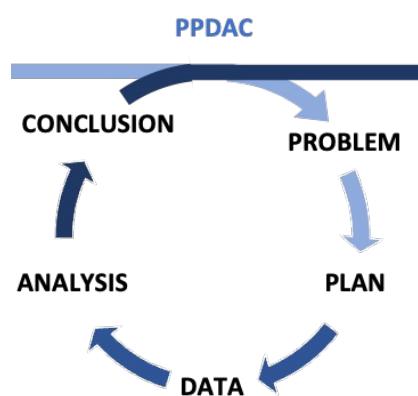
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Learning objectives

By the end of the workshop, you will recognize:

- The integrated set of thinking skills and practices of data science thinking, refocused for answering questions with data.
- It is essential to have a clear understanding of the problem to provide an impactful solution.
- Strategies for problem formulation and how using these tactics is important before delving into solutions.
- The key skill of asking great questions in understanding the problem and its context, as well as in establishing trust and building relationships.
- How question framing helps in defining the broader problem, which has a domino effect on the subsequent workflow phases.



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Introduction

Motivating the data science thinking process

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Why this course?

This is your Machine Learning System?

What if the answers are wrong?

Yup! You pour the data into this big pile of math, then collect the answers on the other side.

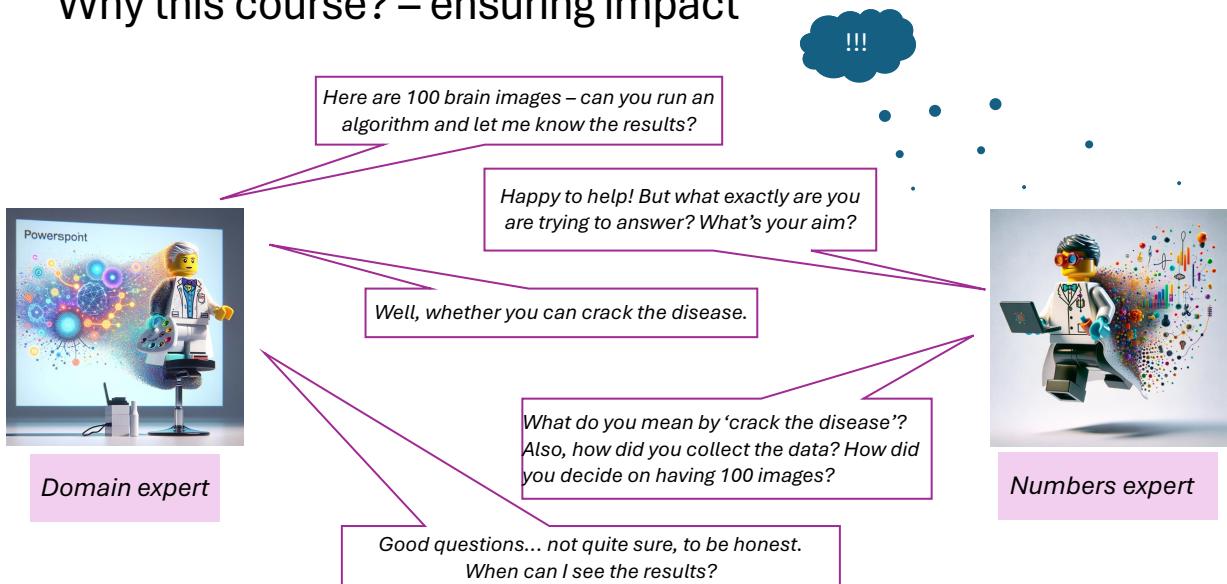
Just stir the pile until they start looking right.

Credit: <https://xkcd.com/1838/> (adapted)

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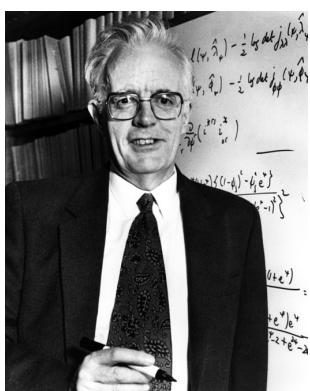
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Why this course? – ensuring impact



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Why this course? – Avoiding Type III errors



In all fields of work, even in pure mathematics, the formulation of issues or questions for investigation is central. Better a rough answer to an **important issue** than a beautiful study of a **topic of no real concern**. Statistical considerations enter in at least two ways. The first is to ensure that the questions are **reasonably defined and capable of being addressed**. Then, do we have or can we collect **data capable of giving a reasonable answer**?

Sir David Cox (2017)

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Why this course? – ensuring impact

npj | precision oncology

Published in partnership with The Hormel Institute, University of Minnesota

Comment



<https://doi.org/10.1038/s41698-024-00553-6>

All models are wrong and yours are useless: making clinical prediction models impactful for patients

Florian Markowetz

Check for updates

Most published clinical prediction models are never used in clinical practice and there is a huge gap between academic research and clinical implementation. Here, I propose ways for academic researchers to be proactive partners in improving clinical practice and to design models in ways that ultimately benefit patients.

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Data Science

Motivating the data science thinking process

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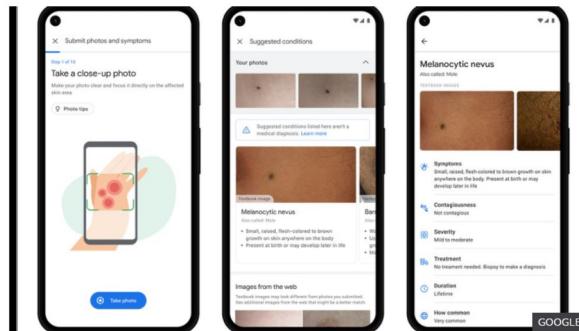
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Advances in data science

Google AI tool can help patients identify skin conditions

By Zoe Kleinman
Technology reporter

① 20 hours ago



Google has unveiled a tool that uses artificial intelligence to help spot skin, hair and nail conditions, based on images uploaded by patients.

Source: <https://www.bbc.com/news/technology-57157566>

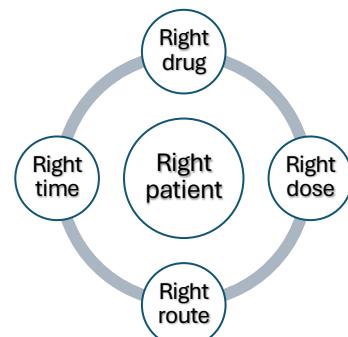


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Can “data science” accelerate drug development?

By **learning from existing and future data** using advances in science, statistics, machine learning, computation, AI, etc. to:

- Increase understanding of drug, disease and patients,
- accelerate and improve development projects,
- inform decision making.



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Many questions in drug development

Leveraging Data Science in Drug Development

- **Treatment effect heterogeneity:** Who will respond better?
- **Disease Progression:** Better measures of disease/disability progression?
- **Clinical prediction:** What are the disease risk predictors?
- **Digital Sensors:** decentralised patient measurements?
- **Informative outcomes:** Developing and validating endpoints

Frontiers of Data Science:

- Causal Inference
- Multi-Modal Inference
- AI & medical devices
- Synthetic and Historical Controls
- Digital Twins

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By learning from existing and future data using advances in science, statistics, machine learning, computation, AI, etc. to:

- increase our understanding of drug, disease and patients,
- accelerate and improve our development projects, and
- inform our decision making.

What do we mean by data science?

What are the practices of data science?

What do we mean by “good” practice in the context of drug development?

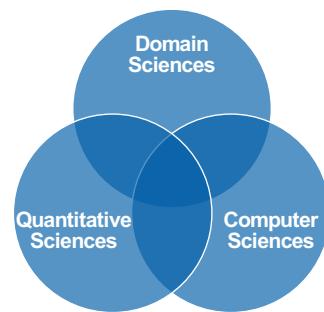
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What is Data Science?

“ *Data science is the study of extracting value from data.* **”** – Jeannette Wing¹

- Data science is an interdisciplinary field to facilitate learning from data
- Impactful data science projects are **cross-functional** efforts
- The technical foundations of data science draw on quantitative and computer sciences, used in conjunction with profound domain expertise



¹Source: <https://datascience.columbia.edu/news/2018/what-is-data-science>

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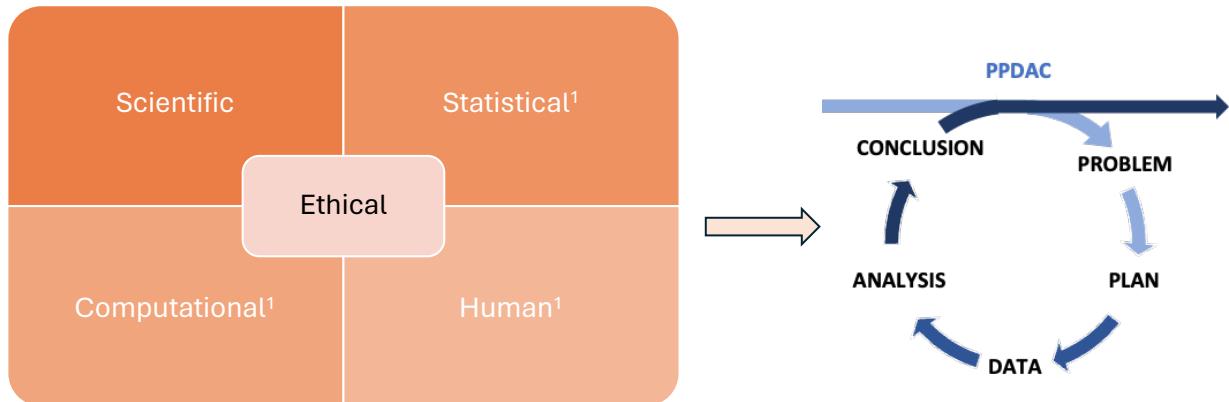
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Data science thinking

A set of integrated thinking skills and practices refocused for answering questions with data



¹ Blei & Smyth (2017) *Science and data science*. PNAS 114 (33):8689-8692

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Why good practice?

A good **workflow** is an established set of habits that help drive you forward towards your goal. They enable complexity to scale in the right areas.

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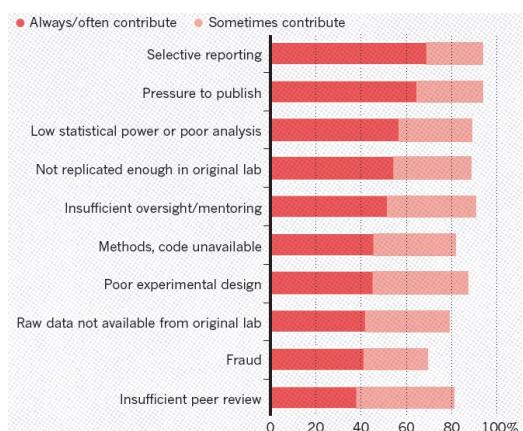
What are the practices of data science?

What factors contribute to irreproducible research?
(Nature's survey of 1,576 researchers)

A crisis facing science?

1,500 scientists lift the lid on reproducibility

Monya Baker survey sheds light
on the 'crisis' rocking research.



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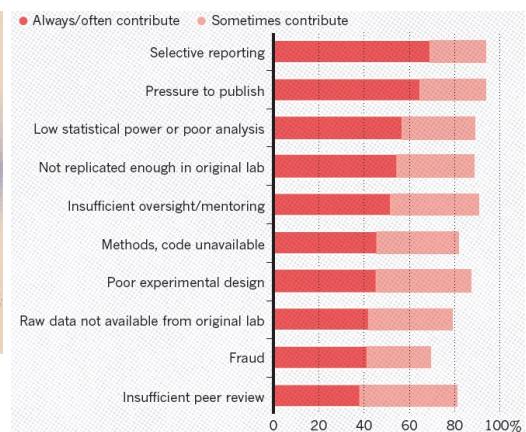
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What are the practices of data science?

- Computational
- Statistical
- Scientific
- Ethical and legal
- Human



What factors contribute to irreproducible research?
(Nature's survey of 1,576 researchers)



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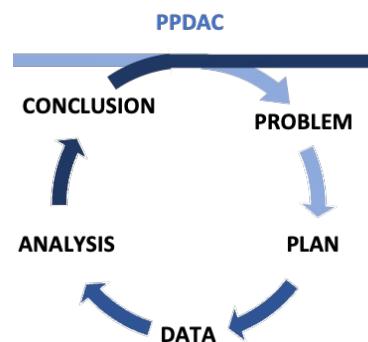
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Data Science Thinking Process

How to make an impact

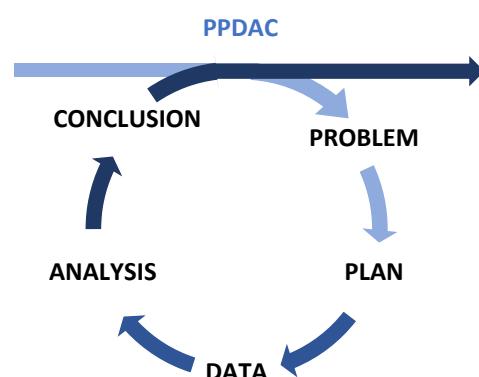
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Data science thinking process

The recipe to ensure impact:

- A clearly motivated problem
- A well-defined question(s)
- Quality data and valid analysis strategy
- Smooth execution
- Appropriate evaluation, and
- Effective communication of outcomes



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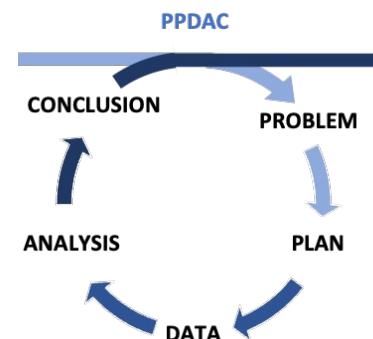
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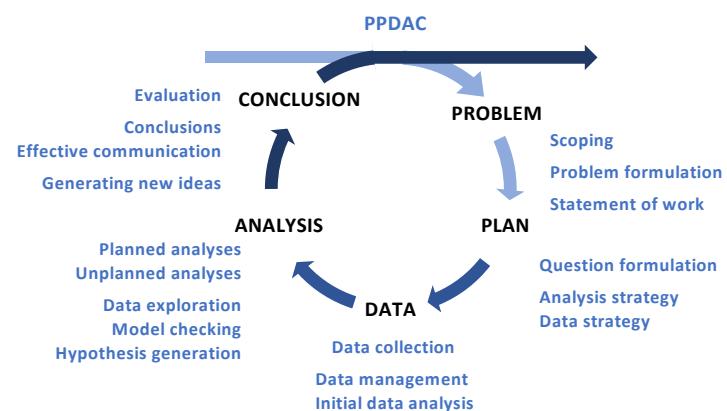


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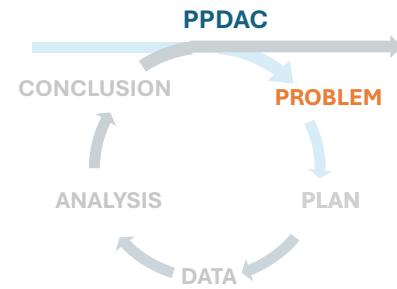
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Data science thinking process



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Problem

- elicit and understand the problem
- asking great questions
- translating into answerable questions

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The importance of problem formulation

"we can't stress this enough – you simply must understand the real problem if you hope to help solve it." (Ron Kenett and Thomas C. Redman)

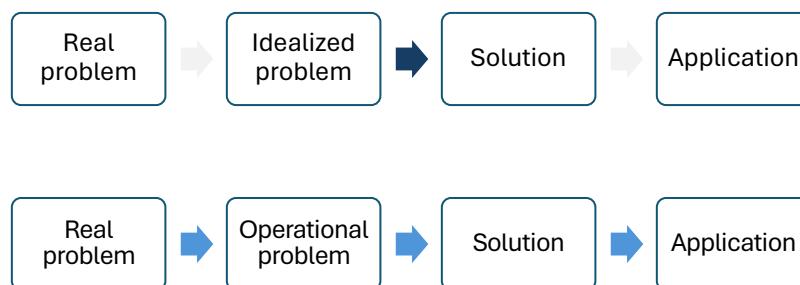
- **From Aim to Question:** Translate high-level aims into tangible, answerable questions.
- **Context Comprehension:** Strive to grasp the full scope, aims, objectives, and constraints
- **Objectives vs Questions:** Differentiate broad research aims from specific, data-driven (research) questions
- **Initial Scoping:** Investigate the context thoroughly to inform objectives and outcomes
- **Critical Questioning:** Ask expansive questions to preclude Type III errors and gain essential domain understanding to help formulate answerable questions.
- **Multiple Pathways:** At this phase explore various approaches to achieving project aims.

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Why? - impact and problem formulation

"I have never let my schooling interfere with my education." Mark Twain



<https://rss.onlinelibrary.wiley.com/doi/epdf/10.1111/1467-9884.00130>

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Philosophy of language

- A young married couple move into a new apartment and decide to repaper the dining room.
- They call on a neighbor who has a dining room the same size and ask:
- **"How many rolls of wallpaper did you buy when you papered your dining room?"**
- "Seven," he says.
- So the couple buys seven rolls of expensive paper, and they start papering.
- When they get to the end of the fourth roll, the dining room is finished.



h/t Miguel Hernán

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Asking the wrong question

- Annoyed, they go back to the neighbor and say,
- “We followed your advice, but we ended up with three extra rolls!”
- “So,” he says, “that happened to you too.”
- Oops!

“How many rolls of wallpaper **did you** buy when you papered your dining room?”



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Problem formulation: tactics

- **Objective:** Gain a thorough understanding of the problem, its context, and potential impact.
- **Engage with experts:** Identify and clarify crucial details with domain experts:
 - Purpose, objectives, and expected outcomes.
 - Investigation phases and types.
 - Attributes vital for crafting focused questions.
 - Project boundaries and constraints.
- **Strategize information gathering:**
 - Formulate effective tactics to collect information efficiently.
 - “asking great questions” (Vance et al. 2022)
- **Questioning techniques:** Employ probing questions to convert domain expertise into precise research questions.
- **Communicate effectively:** Use clear, direct language to foster understanding and build trust.

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Bad, good and great questions

1. So that we do not waste any more time, what is the exact statistics question you need my help answering?
2. With respect to the scientific area to which these ideas refer, just what are they about?
3. My goal for this initial meeting is to understand your research problem better, which will help me think about the specific statistical issues. What would you like to accomplish in this meeting?

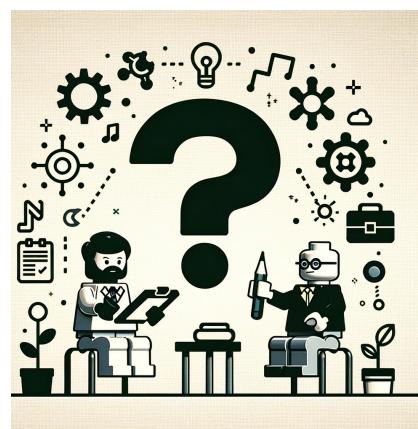


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Asking great questions

- Great questions (Vance et al., 2022)
 - elicit information useful for accomplishing project tasks
 - Strengthen team relationships and understanding
 - i.e. better understanding between "domain" and "number" experts
- Great questions have 3 parts:
 - The question
 - The answer
 - Paraphrasing the answer to create shared understanding
- Strategies
 - Preface questions with intent behind asking the question

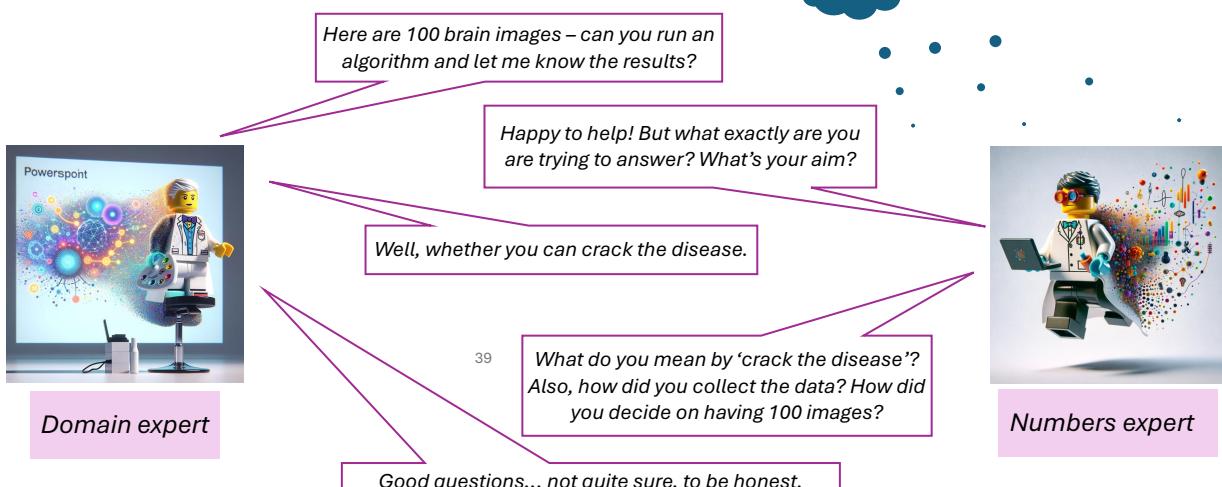


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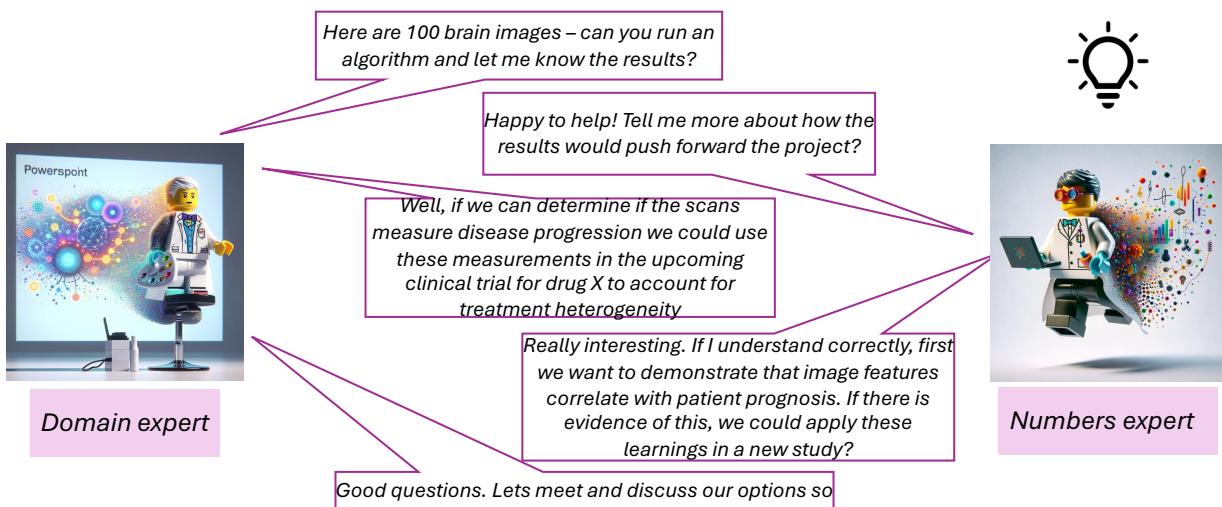
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Asking good questions



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Asking great questions

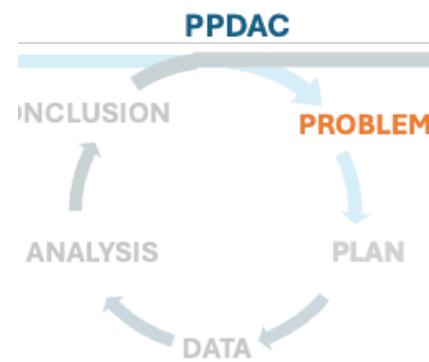


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Summary

- Problem formulation
 - “we can't stress this enough – you simply must understand the real problem if you hope to help solve it.” (Ron Kenett and Thomas C. Redman)
- Ask probing questions for understanding context and elicit key information
- Asking effective questions is a key competency during the problem phase
- Next step – we will outline a framework to help formulate which questions to ask to define “answerable” questions

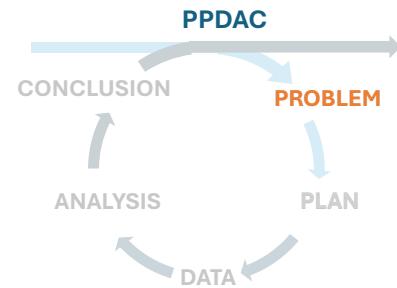


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Problem

- scoping
- statement of work
- clear thinking, transparency, reproducibility & knowledge transfer



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Which information do we need to clarify?

Last section we highlighted the importance of problem formulation and how “great questions” can help with understanding the context.

The aim was to formulate a problem clearly

- But what questions to ask?
- What information is important to find out?

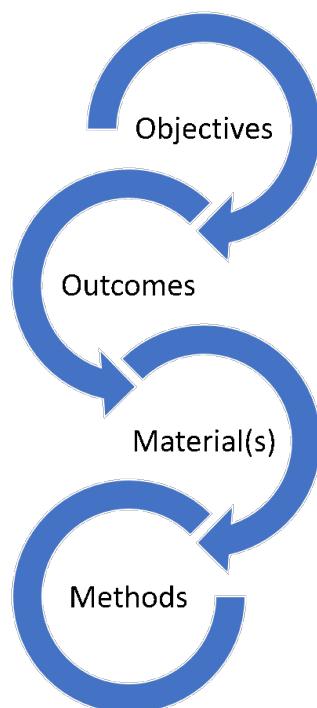
Now we provide a structured framework for obtaining this key information. This is often called the process of “scoping”

We also provide a statement of work (SoW) template to help collect this information systematically

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The iterative steps of scoping



1. Objectives(s) – capture, define and refine the goal and objective(s) of the project;
2. Outcome(s) – capture what actions, decisions or interventions will the outcome of the project inform;
3. Materials – what data and other resources are required to achieve these goals;
4. Methods –
 - What analyses need to be performed?
 - What analysis type(s) and strategies are required (describe, detection, prediction, intervention, explanation? (Hernán et al. 2019)).

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Type of question (the zeroth problem)



Descriptive

Provide insight into the past and answer: 'What has happened?'

- How many females under the age of 50 were enrolled into the study?



Predictive

Understand the future and answer: 'What could happen?'

- What is the probability of having a cardiovascular event in the next 3 years for females with specific characteristics?



Prescriptive

Describe causal relationships and answer: 'What should we do?'

- Will prescribing Super Drug X reduce the risk of a cardiovascular event, on average, compared to staying on the current standard of care?

Hernan et al. (2019), Mallows (1998), Shmueli (2010)

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Enhancing Impact with a Statement of Work

• SoW Objectives:

- Ensure alignment of business and scientific inquiries with actionable plans
- Facilitate knowledge transfer and enhance project oversight

• Document essentials:

- Project purpose, background, and detailed objectives.
- Expected outcomes and methodologies.
- Governance structure, team roles, and contribution details.
- Defined timelines with critical milestones.

• Knowledge Management:

- Capture and store project details for easy retrieval.
- Enable efficient knowledge sharing and continuity.

• Benefits:

- Provides a framework for reproducibility and systematic execution
- Accessible SoW allows for comprehensive project tracking and transparency

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SoW – available online

<https://github.com/datascience-thinking/SoW>

GDSP statement of work (SOW)

Document goal: Ensure the right business and scientific questions are formulated, and the right analyses are designed to address these questions, and assess necessary resources identified to plan and execute plans.

Output: a brief written description of the questions to be addressed, the activities to address them and who was involved in this assessment. GDSP SOW should be stored on a knowledge management system, with the location of the document captured in a tracker.

Revision tracking: The GDSP SOW should be maintained to capture major changes in project scope during execution and completion. A change log is available to capture this information.

PROJECT INFORMATION

Project Title	Provide a descriptive project title.
Project code / identifier (if applicable)	Add the project code or identifier in here if one exists. This will help with retrieval of the project materials.
Project requestor / sponsor (if applicable)	Add details of the requestor i.e. principal investigator, business unit, etc.
GxP applicability?	Indicate if this work is purely exploratory (and for internal purposes only) or if the project outcomes could be subject to regulatory interactions, part of a submission to a health authority, to a scientific publication, etc. The purpose is to help discussion and planning around potential verification and validation activities, and especially to avoid rework later.
Project keywords	Add keywords to help with retrieval of the project.

PURPOSE & BACKGROUND

Provide an informal summary of the scientific/business context, and what is known about the situation at the beginning of the project. Point out the value added, including the scientific and business impact for your organization, with a clear business justification for why the project is needed? Also, provide a rationale in terms of what is already known about the problem and what gaps exist (i.e. why this project is required). It may be helpful to answer the following questions when filling out this section:

- What problem is this project solving?
- How do we know this is a real problem and worth solving?

Capture the details of any background research performed such as project identifiers or links to useful resources. It is useful to capture references to previous relevant projects, or similar work performed, to ensure existing materials and resources are utilized, as well as connecting projects to support future knowledge management and discovery.

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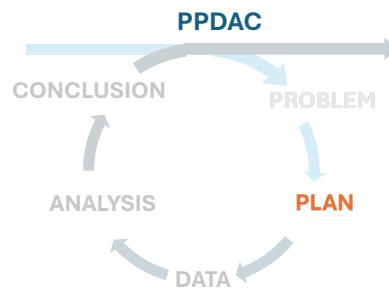
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Summary, scoping & statement of work

- **Scoping:**
 - Provides a structured approach for eliciting crucial problem-formulating information.
 - What are the areas to focus on for information gathering
- **Iterative Process:** Encourages regular refinement and documentation for clarity and direction.
- **Documentation benefits:**
 - Enhances reproducibility and transparency within the team.
 - Assists in identifying and mitigating assumptions and biases.
- **Best Practices:** considered essential and ethical across various sectors for robust project management.

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Plan

- getting the question(s) right

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Plan: getting the questions right

- Moving from **problem** formulation into analysis strategy – how to solve problems
- The **problem** phase helps with framing the questions and defining the broader problem
- Why is this important? An ‘open-ended’ or “vague” question can be a reason for a failed project
- Getting the questions right has a domino effect on the subsequent steps, such as **data** strategy, **analysis** strategy, **conclusions** & communication
- In practice, it will involve an **iterative** process
 - Do not let the **data** strategy or **analysis** strategy dictate the question!
 - Data, question, analysis all tightly linked and influence each other
 - Questions that can only be answered if data can be collected
 - Analyses may have to adjust for biases in the data

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Principles for formulating a question



Clarify

Ask focused questions in order to clarify the question sufficiently?
Develop a strategy to obtain the necessary information (population, comparison, etc.)



Answerable

Need to have an answerable question by applying an iterative, hierarchical approach to start from a high-level question and end with a reasonably granular, answerable question



Question before solution

Distinction between descriptive / predictive / prescriptive questions; recognize that the same data can answer different questions



Factorial principle

May have multiple questions; need to prioritize and **document** them

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Thought experiment¹

Assume we are interested in solving an immediate **health crisis in 1872**:

Does exposure to water have an effect on risk of death among London residents?

Or, for brevity, '**Does water kill?**'

Is this question precise enough?



Source: ¹Hernan (2016): <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5207342/pdf/nihms836995.pdf>

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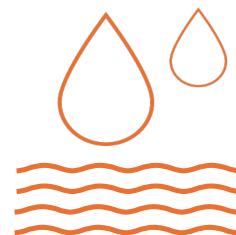
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Version #1

Does water kill?

Do we mean:

- Immersion (death by drowning)
- Flash flood (death by trauma), or
- Drinking water (death by poisoning)?



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Version #2

Does **drinking** water kill?

We mean fresh water, not salty water.



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Version #3

- Does drinking **fresh** water kill?

How much water?

10 liters per day will kill you...



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Version #4

- Does drinking **a large sip** of fresh water kill?

What is the source of the water?

Tap, fountain, directly from the river...



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Version #5

- Does drinking a large sip of fresh water from the Broad Street pump kill?
- Are we talking under 1871 conditions, or 1872 when drinking water regulations looked very different?



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Version #6

- Does drinking a large sip of fresh water from the Broad Street pump in 1872 kill?
- Ok, but compared with what? With drinking 3 liters of beer?

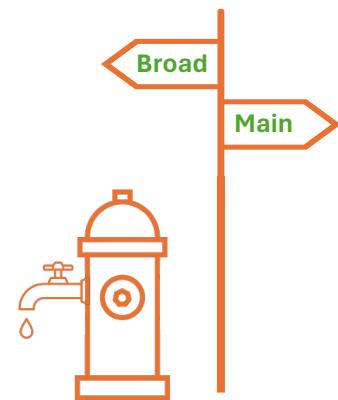


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Version #7

- Does drinking a large sip of fresh water from the Broad Street pump in 1872, compared to drinking all your water from the Main Street pump, kill?
- What about other concomitant factors that may affect your outcome of interest?

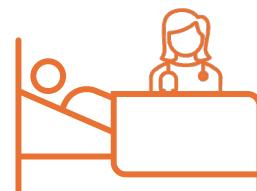


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Version #8

- Does drinking a large sip of fresh water from the Broad Street pump in 1872 and not initiating a rehydration treatment if diarrhea occurs, compared to drinking all your water from the Main Street pump, kill?
- And so on ...



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Version #1'000'000

- [very
long
text
goes
here]

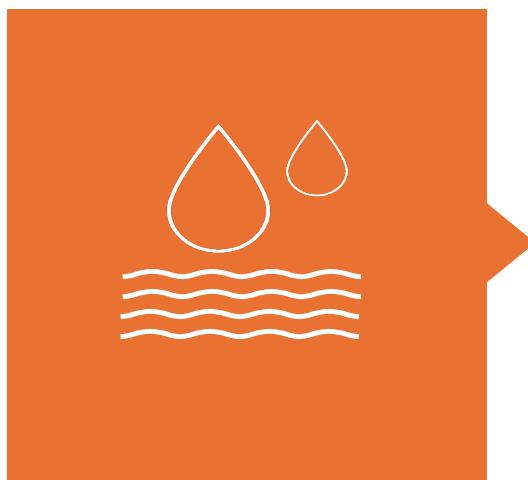


- Is Version #1'000'000 precise enough?
 - ✓ No version of the question is perfectly well-defined
 - ✓ Fortunately, absolute precision is not necessary
 - ✓ Further specification is required only while meaningful vagueness remains
 - For example, we may not believe the speed of the water from the pump would lead to different conclusions → no need to specify the water speed

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Summary 1/2



The original question was hopelessly vague because there are many possible versions of 'water' and 'kill'

Certain degree of vagueness remains despite our efforts to refine the question. However, we can start to design how to answer version #8 than with versions #1 and #2

Many versions of 'water' are irrelevant (e.g., the speed at which water flowed) and therefore do not bother to specify them

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Summary 2/2



Likewise, the question

'Does obesity kill?'

is hopelessly vague as well because there are many possible versions of 'obesity' and 'kill.'

Is more **appropriate question:**

Would the 20-year death risk differ if the human population of interest were assigned to gaining weight **by force feeding** 5000 vs. 2500 calories per day between ages 30 and 50?

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Where are we?



What we have learned so far:

Questions are often too vague and need to be refined iteratively to make them precise enough.

What comes next:

Recognize that
... different types of questions are possible

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Type of question (revisited)



Descriptive

Provide insight into the past and answer: 'What has happened?'

- How many females under the age of 50 were enrolled into the study?



Predictive

Understand the future and answer: 'What could happen?'

- What is the probability of having a cardiovascular event in the next 3 years for females with specific characteristics?



Prescriptive

Describe causal relationships and answer: 'What should we do?'

- Will prescribing Super Drug X reduce the risk of a cardiovascular event, on average, compared to staying on the current standard of care?

Hernan et al. (2019), Mallows (1998), Shmueli (2010)

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Example thinking frameworks (estimands)

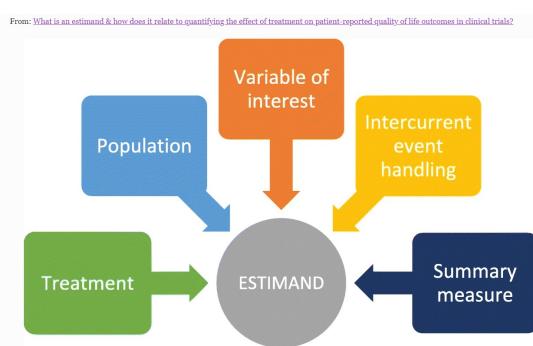


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 30 August 2017
2 EMA/CHMP/ICH/436221/2017
3 Committee for Human Medicinal Products

4 ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials

[ICH E9 \(R1\) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials - Step 2b \(europa.eu\)](#)



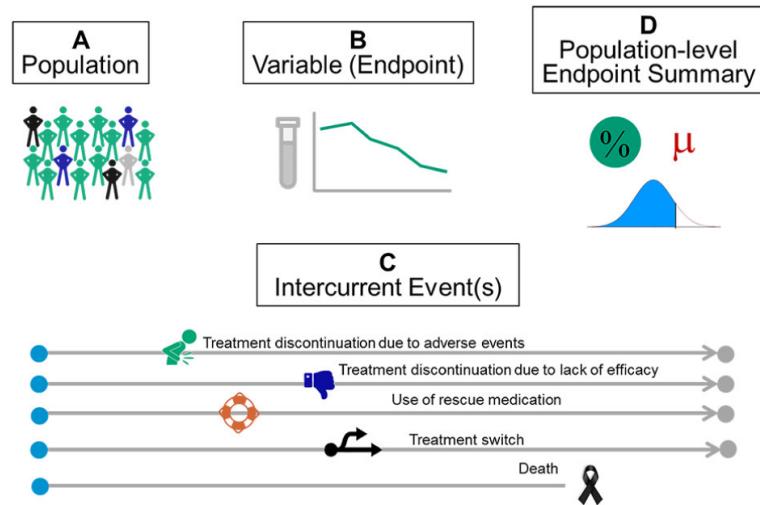
Lawrence, R., Degtyarev, E., Griffiths, P. et al.

What is an estimand & how does it relate to quantifying the effect of treatment on patient-reported quality of life outcomes in clinical trials?. J Patient Rep Outcomes 4, 68 (2020). <https://doi.org/10.1186/s41687-020-00218-5>

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Attributes for formulating the estimand



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Strategies for addressing intercurrent events in the scientific question of interest

Strategy	Example of Endpoint or Effect of Interest
Treatment Policy	Overall survival regardless of whether or when treatment switching happens
	Treatment switch
Composite	Viral rebound or treatment discontinuation due to AE
	Treatment discon due to AE
Hypothetical	Change in HbA1c if rescue medication is not allowed
	Switch to rescue medication
Principal Stratum	Infection severity in subpopulation that will become infected despite preventive treatment
While on Treatment	Quality of life during palliative care treatment until death
	Death

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Example thinking frameworks: The PICO question statement

Question Type	Patient or Problem	Intervention or Exposure	Outcome	Comparison
Therapy	In patients with hypertension and at least one additional cardiovascular disease risk factor	Does tight systolic blood pressure control	Lead to lower rates of myocardial infarction, stroke, heart failure, and cardiovascular mortality	Compared to conservative control?
Diagnosis	Among asymptomatic adults at low risk of colon cancer	Is fecal immunochemical testing (FIT)	As sensitive and specific for diagnosing colon cancer	As colonoscopy?
Prognosis	Among adults with pneumonia	Do those with chronic kidney disease (CKD)	Have a higher mortality rate	Than those without CKD?
Etiology or Harm	Are women	With a history of pelvic inflammatory disease (PID)	At higher risk for gynecological cancers	Than women with no history of PID?
Prevention	Among adults with a history of myocardial infarction	Does adherence to a mediterranean diet	Lower risk of a second myocardial infarction	Compared to those who do not adopt a mediterranean diet?

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Target trial emulation

<https://academic.oup.com/aje/article/183/8/758/1739860>

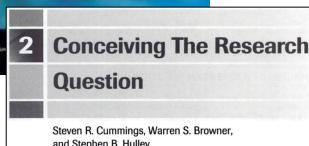
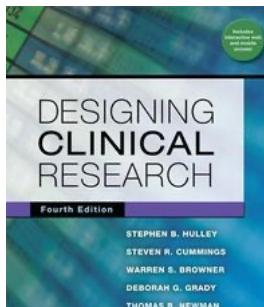
Table 1.
A Summary of the Protocol of a Target Trial to Estimate the Effect of Postmenopausal Hormone Therapy on the 5-Year Risk of Breast Cancer

Protocol Component	Description
Eligibility criteria	Postmenopausal women within 5 years of menopause between the years 2005 and 2010 and with no history of cancer and no use of hormone therapy in the past 2 years.
Treatment strategies	Refrain from taking hormone therapy during the follow-up. Initiate estrogen plus progestin hormone therapy at baseline and remain on it during the follow-up unless you are diagnosed with deep vein thrombosis, pulmonary embolism, myocardial infarction, or cancer.
Assignment procedures	Participants will be randomly assigned to either strategy at baseline and will be aware of the strategy to which they have been assigned.
Follow-up period	Starts at randomization and ends at diagnosis of breast cancer, death, loss to follow-up, or 5 years after baseline, whichever occurs first.
Outcome	Breast cancer diagnosed by an oncologist within 5 years of baseline.
Causal contrasts of interest	Intention-to-treat effect, per-protocol effect
Analysis plan	Intention-to-treat effect estimated via comparison of 5-year cancer risks among individuals assigned to each treatment strategy. Per-protocol effect estimation requires adjustments for pre- and postbaseline prognostic factors associated with adherence to the strategies of interest. All analyses will be adjusted for pre- and postbaseline prognostic factors associated with loss to follow-up (57). This analysis plan implies that the investigators prespecify and collect data on the adjustment factors.

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Many existing frameworks



ACP Journal Club

The well-built clinical question: a key to evidence-based decisions

Author(s): Richardson, W. Scott MD; Wilson, Mark C. MD, MPH; Nishikawa, Jim MD; Hayvard, Robert S. A. MD, MPH
Issue: Volume 123, Nov-Dec 1995, pp A-12
Publication Type: [Editorial]
Publisher: Copyright (C) 1995 American College of Physicians. All Rights Reserved.

ISSN: 12345678
Accession: 00021607-199511000-00027

ICH
International Council for Harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

ADDENDUM ON ESTIMANDS AND SENSITIVITY ANALYSIS IN CLINICAL TRIALS TO THE GUIDELINE ON STATISTICAL PRINCIPLES FOR CLINICAL TRIALS
E9(R1)

Fast version
Adopted on 20 November 2019

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory partners, in accordance with the ICH Process. At Day 0 of the Process the final draft is recommended for adoption in the regulatory bodies of the ICH regions.

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Principles for formulating a question



Clarify

Ask focused questions in order to clarify the question sufficiently? Develop a strategy to obtain the necessary information (population, comparison, etc.)



Answerable

Need to have an answerable question by applying an iterative, hierarchical approach to start from a high-level question and end with a reasonably granular, answerable question



Question before solution

Distinction between descriptive / predictive / prescriptive questions; recognize that the same data can answer different questions



Factorial principle

May have multiple questions; need to prioritize and document them

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Summary

The primary importance of framing the questions is that it narrows down a real problem of interest into a specific answerable task

- Framing the questions helps defining the broader problem
- Getting the questions right has a domino effect on the subsequent steps highlighted in the workflow
- A vague ‘open-ended’ question can be a reason for a failed project
- For many problems, it is wise to ask a series of interrelated questions rather than a single question

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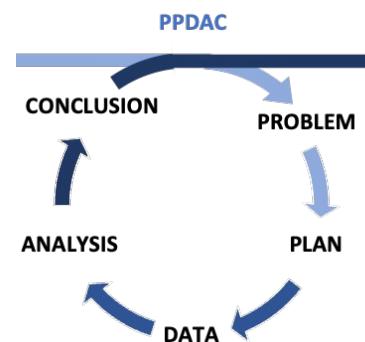
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Data science thinking process

A set of integrated **thinking skills** and practices refocused for answering questions with data

A good **workflow** is an established set of habits that help drive you forward towards your goal. They enable complexity to scale in the right areas.

This workflow demonstrates the steps for abstracting and solving a **real problem**. An impactful solution requires a clear understanding of how things work.



Source: MacKay, R.J. and Oldford, R.W., 2000. Scientific method, statistical method and the speed of light. *Statistical Science*, pp.254-278.

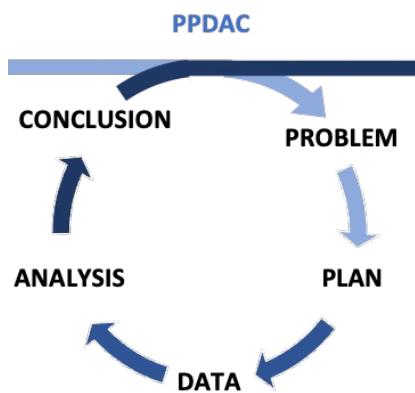
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Learning objectives

By the end of the workshop, you will recognize:

- The integrated set of thinking skills and practices of data science thinking, refocused for answering questions with data.
- It is essential to have a clear understanding of the problem to provide an impactful solution.
- Strategies for problem formulation and how using these tactics is important before delving into solutions.
- The key skill of asking great questions in understanding the problem and its context, as well as in establishing trust and building relationships.
- How question framing helps in defining the broader problem, which has a domino effect on the subsequent workflow phases.



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Any Questions?



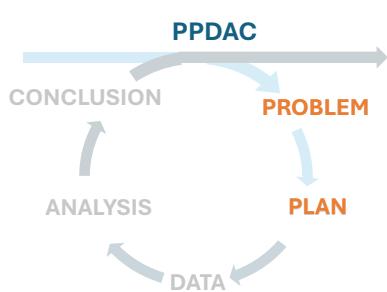
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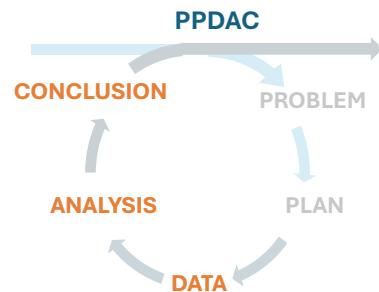
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Data science thinking: making an impact

Part I



Part II



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References & Further Reading Material



References:

- Cox (2017) Statistical Science: A Grammar for Research. European Journal of Epidemiology 32: 465–71. <https://doi.org/10.1007/s10654-017-0288-1>.
- Cummings et al. (2007) Conceiving The Research Question In: Hulley et al (editors) Designing clinical research ([link](#))
- International Council for Harmonisation (2019) ICH E9(R1): Estimands and sensitivity analysis in clinical trials. ([link](#))
- Richardson et al. (1995). The well-built clinical question: A key to evidence-based decisions. ACP Journal Club, 123, A12-13. <https://doi.org/10.7326/ACPJC-1995-123-3-A12>
- Vance et al. (2022) Asking great questions. *Stat*, 11(1), p.e471.
- Kenett, R.S. and Redman, T.C., 2019. *The real work of data science: turning data into information, better decisions, and stronger organizations*. John Wiley & Sons.
- Hernán, M.A., Hsu, J. and Healy, B., 2019. A second chance to get causal inference right: a classification of data science tasks. *Chance*, 32(1), pp.42-49
- Shmueli, Galit. "To explain or to predict?." (2010): 289-310.

Further reading material:

- Bouchrika (2023) How to write a research question: Types, steps, and examples. <https://research.com/research/how-to-write-a-research-question>
- Haynes (2006) Forming research questions. *Journal of Clinical Epidemiology* 59: 881–86. <https://doi.org/10.1016/j.jclinepi.2006.06.006>
- Mallows (1998) The Zeroth Problem. *The American Statistician* 52: 1–9. <https://doi.org/10.1080/00031305.1998.10480528>.

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Build upon these works ...



Good Data Science Practice: Moving Toward a Code of Practice for Drug Development

Mark Baillie ✉ ⓘ, Conor Moloney, Carsten Philipp Mueller, Jonas Dorn ⓘ, Janice Branson & David Ohlssen

Pages 74-85 | Received 16 Jun 2021, Accepted 18 Mar 2022, Published online: 16 May 2022



The Role of Statistical Thinking in Biopharmaceutical Research

Frank Bretz ✉ ⓘ & Joel B. Greenhouse ⓘ

Pages 458-467 | Received 19 Dec 2021, Accepted 19 May 2023, Published online: 24 Jul 2023



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Marc Vandemeulebroecke ✉, Mark Baillie, Alison Margolskee, Baldur Magnusson

First published: 22 July 2019 | <https://doi.org/10.1002/psp4.12455> | Citations: 9

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