

Leveraging Patient-Provided Information to Improve Real-World Evidence – And Vice Versa

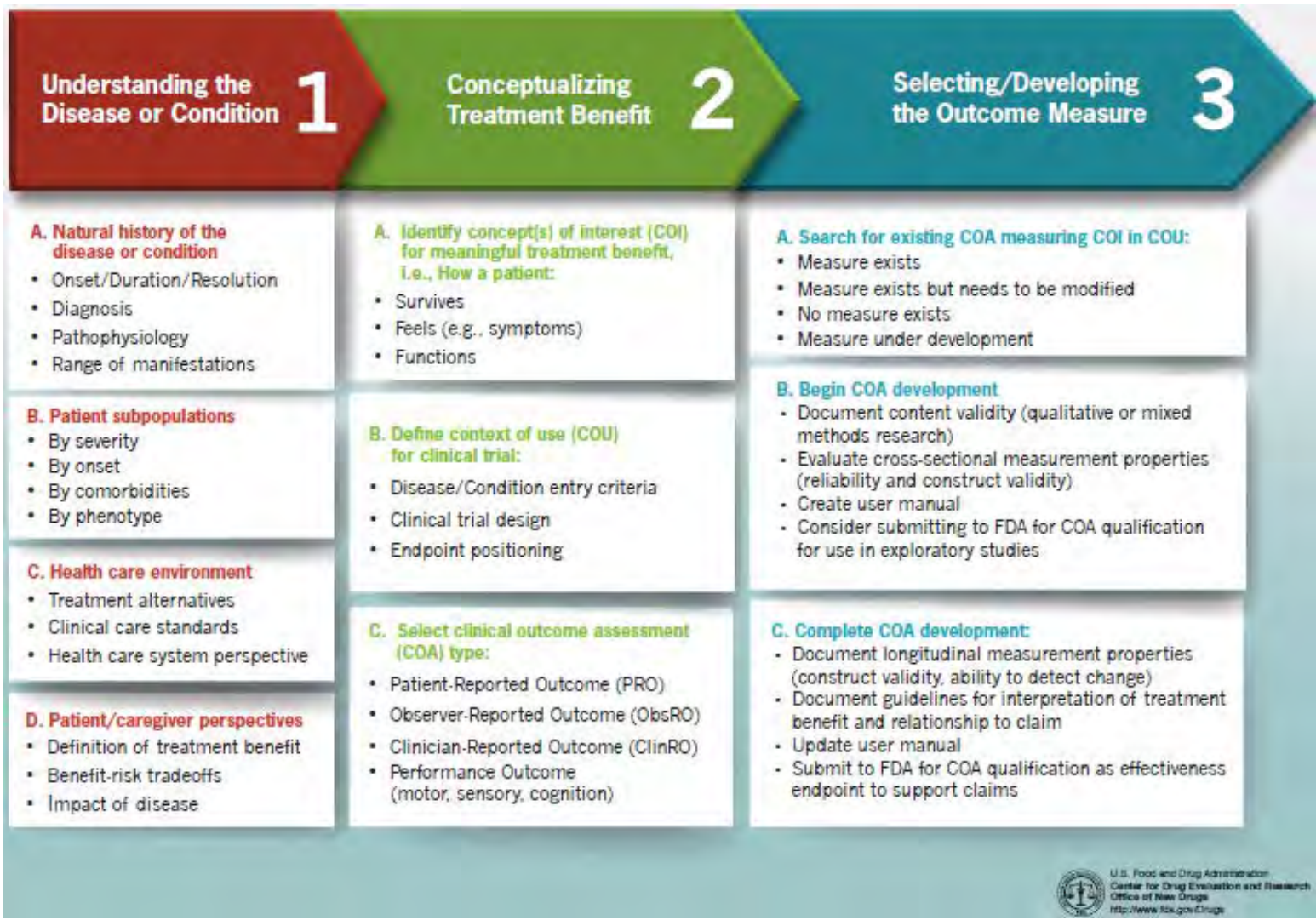
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Starting with the Vice-Versa

**RWE is central to the
FDA Clinical Outcomes Assessment
Roadmap**





RWE + PPI together yield more effective understanding of disease burden and treatment impact



Understanding the disease or condition

- Natural history of the disease or condition
- Patient subpopulations
- Health care environment
- Patient/caregiver perspectives



Conceptualizing treatment benefit

- Identify **Concept Of Interest** for meaningful treatment benefit
- Define **Context of Use**
- Select **Clinical Outcomes Assessment** type



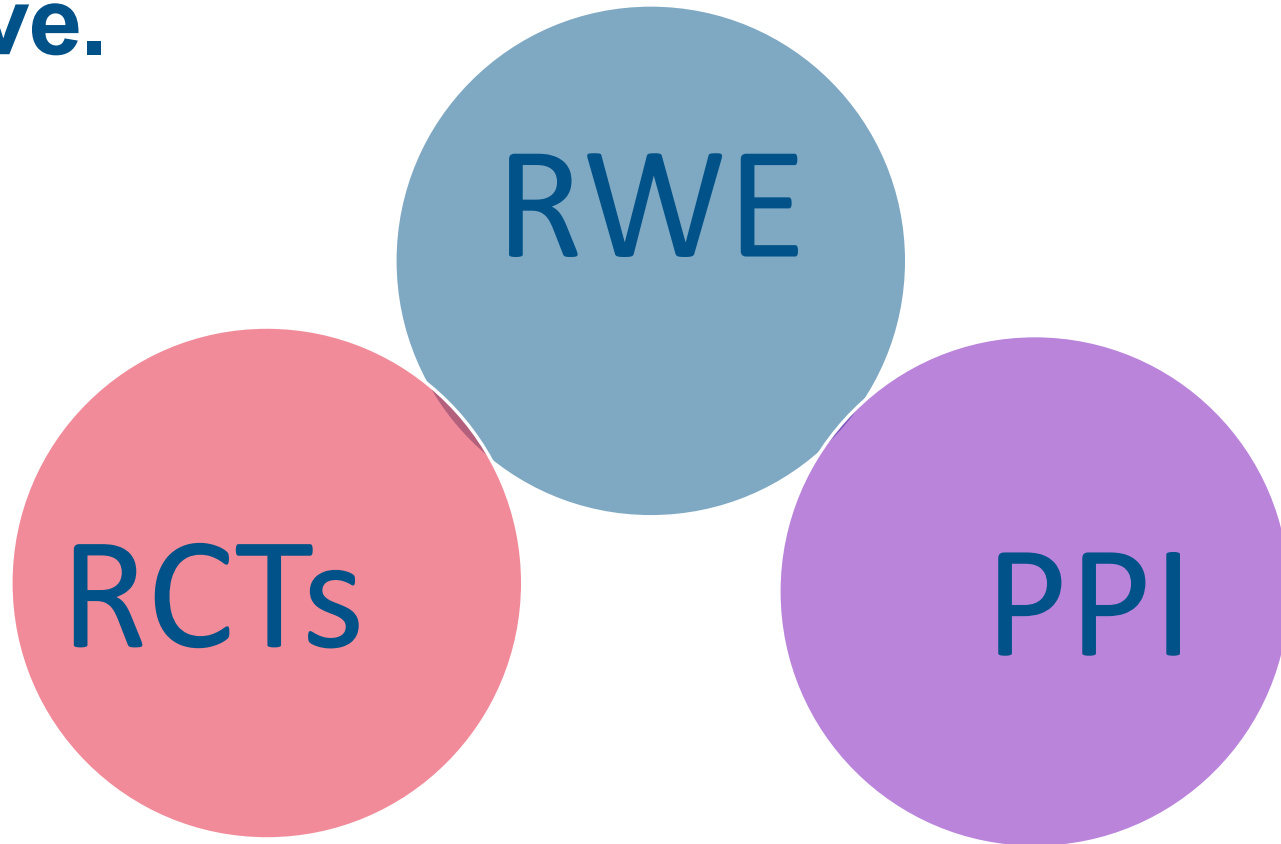
Selecting and developing the outcomes measure

- Search for existing COA measuring COI in COU
- Begin COA development
- Complete COA development

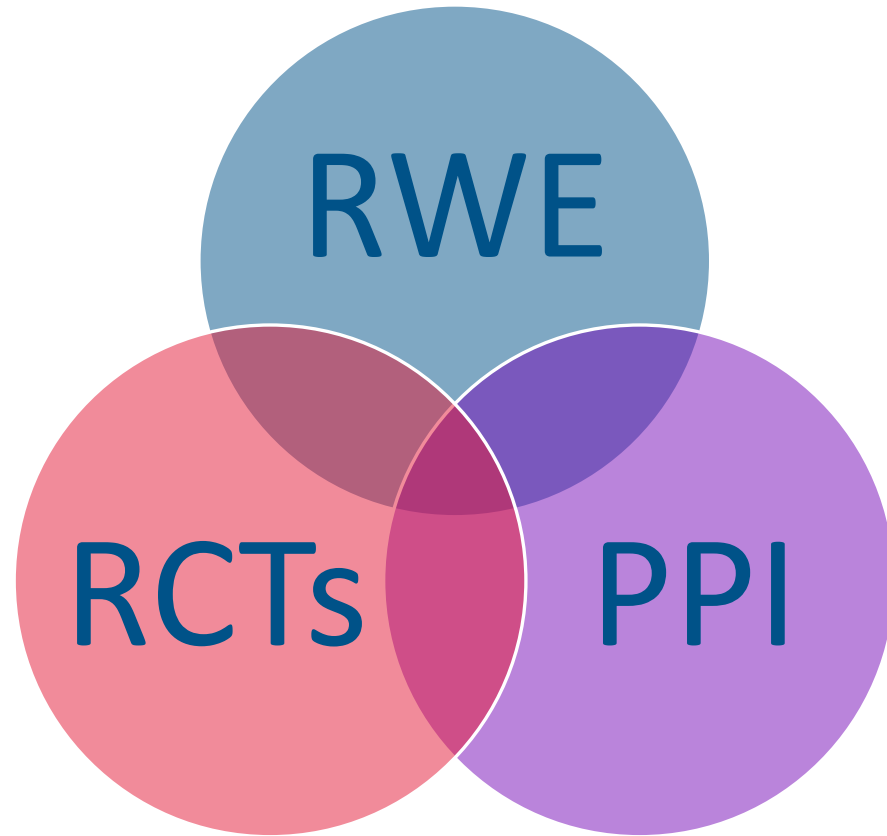
COA=clinical outcome assessment; COI=concept of interest; COU=context of use

<https://www.fda.gov/oc/omb/ais/development/development-process/drug-development-tool-qualification-program/UCM370174.pdf>

Leveraging RWE and PPI can make RCTs and therefore drug development and commercialization more efficient and effective.

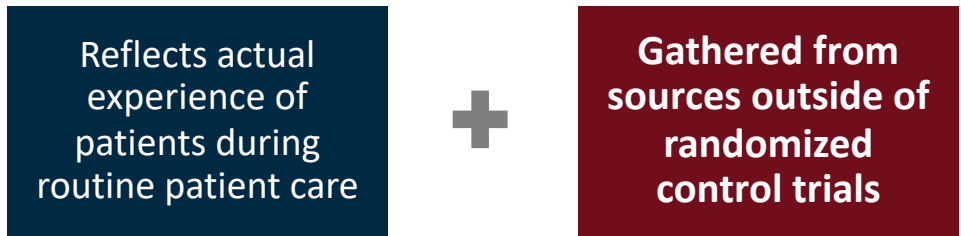


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The Real World Data armamentarium is expanding

Based on recent guidance¹, Real World Data (RWD) typically meets two conditions:



Examples of RWD

Administrative Claims	Clinical EHR	OTHERS
 	 	<ul style="list-style-type: none">• Disease registries• Patient chart reviews• Patient & population surveys• Lab data• Genomic data• Social Media

1. Using Real-World Evidence to Accelerate Safe & Effective Cures , Bipartisan Policy Center, 2016

PPI improves our understanding of Real World disease, healthcare delivery and patient behavior

A real-world study found the perceived importance of factors, which influence the decision to escalate therapy in RA, to differ radically between patients and rheumatologists

Most important reasons to change	Rheumatologist ranking	Patient ranking
Swollen joints	1	12
DAS28 scores	2	17
Rheumatologist impression of overall disease activity	3	8
Worsening erosions past year	4	27
Disease activity now compared to 3 months ago	5	19
Physical functioning and mobility	7	1
Patient's motivation to get better	23	2
Patient's trust in their physician	45	3
Patient's satisfaction with current DMARD	21	4
Painful joints	13	5

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DAS=disease activity score; DMARD=disease-modifying antirheumatic drug; RA=rheumatoid arthritis; RWE=real-world evidence

Source:Van Hulst L, et al. Arthritis Care Res 2011;63(10):1407-14

RWE and PCR can strengthen the efficiency of RCTs



Hypothesis generation

What are appropriate comparator treatment(s)?



Patient identification

What are appropriate inclusion & exclusion criteria? Can these patients be feasibly recruited?



Endpoint clarification

What are relevant outcomes? When and for how long should they be collected?



Prognostic factor identification

Are biomarkers or patient characteristics relevant?



Feasibility determination

Is this study likely to succeed?

Exercise

Hypothetical Study #1

Atrial Fibrillation (AF)

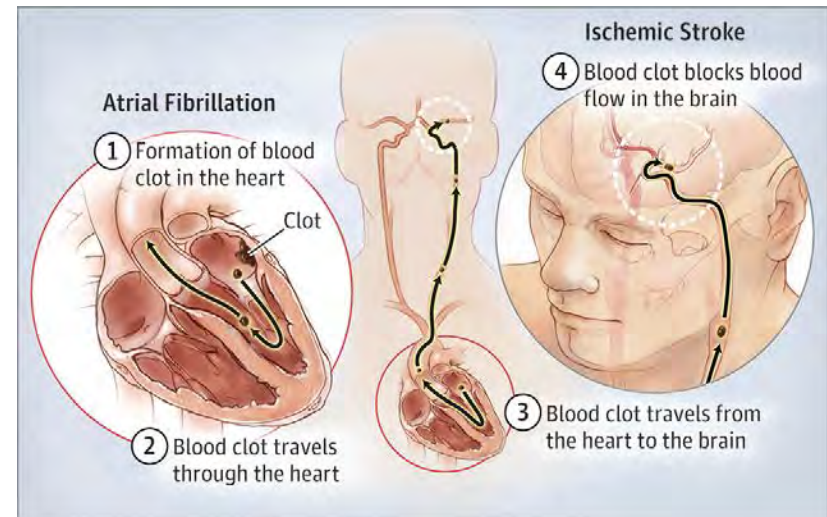
Most common heart rhythm disorder¹

Prevalence of AF increases with age

- Estimated 5% of individuals > 65 years
- Estimated 10% of individuals ≥ 80 ^{2,3}

Independent risk factor for ischemic stroke

- Non-valvular AF patients have 5 times the risk of stroke compared to patients without AF



Source: Berian et al.

Anticoagulants for AF Patients

Oral anticoagulants (OACs) reduce risk of ischemic stroke

- Warfarin, apixaban, dabigatran, edoxaban, and rivaroxaban

Adjusted-dose warfarin reduces stroke risk by ~64% (95% CI: 49, 74)¹

- Novel oral anticoagulants (NOACs) are non-inferior compared to warfarin²
- Stroke rate in AF patients:
 - Untreated 4.4/100 person years
 - Warfarin-treated: 1.6/100 person years³

Increased bleeding risk

- Warfarin: <0.3% per year¹
- Homogenous risk for bleeding
 - Overlapping risk factors

1. Hart RG et al. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med.* . 2007;146:857-867.

2. Adam SS, et al. Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Management of Atrial Fibrillation and Venous Thromboembolism: A Systematic Review. *Ann Intern Med.* 2012;157:796–807.

3. Go AS, et al. The extent of atrial fibrillation in the United States. *Circulation.* 2001;104:50-55.

Patient Provided Information

- Journey to diagnosis can be lengthy and confusing as symptoms can vary substantially between AF patients
 - Include absence of symptoms, vague symptoms such as “effort intolerance,” or unusual symptoms in the chest area, making early diagnosis difficult
- Symptoms may also be confused with other conditions
 - For example, among interviewed patients, three mistook their symptoms for other conditions and sought care for:
 - Suspected heart attack
 - Indigestion
 - Anxiety attack



Hypothetical Study #1

Study Objective:

To study the effectiveness of anticoagulants for reducing stroke among atrial fibrillation patients

Study Type:

Retrospective cohort study

Question:

How would this patient-provided information impact your decision-making throughout the steps outlined in the research design framework?



Patient-provided Input:

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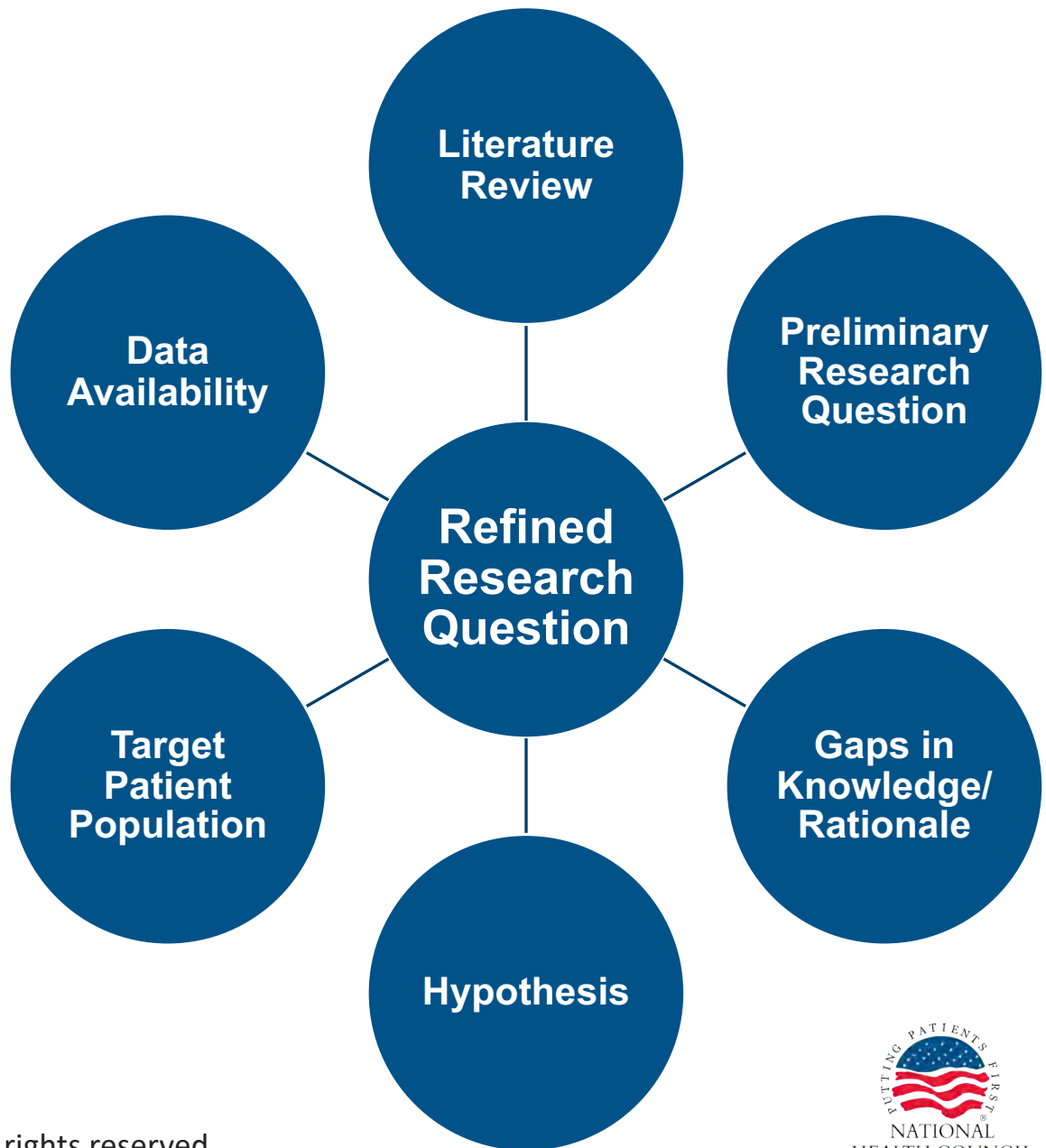
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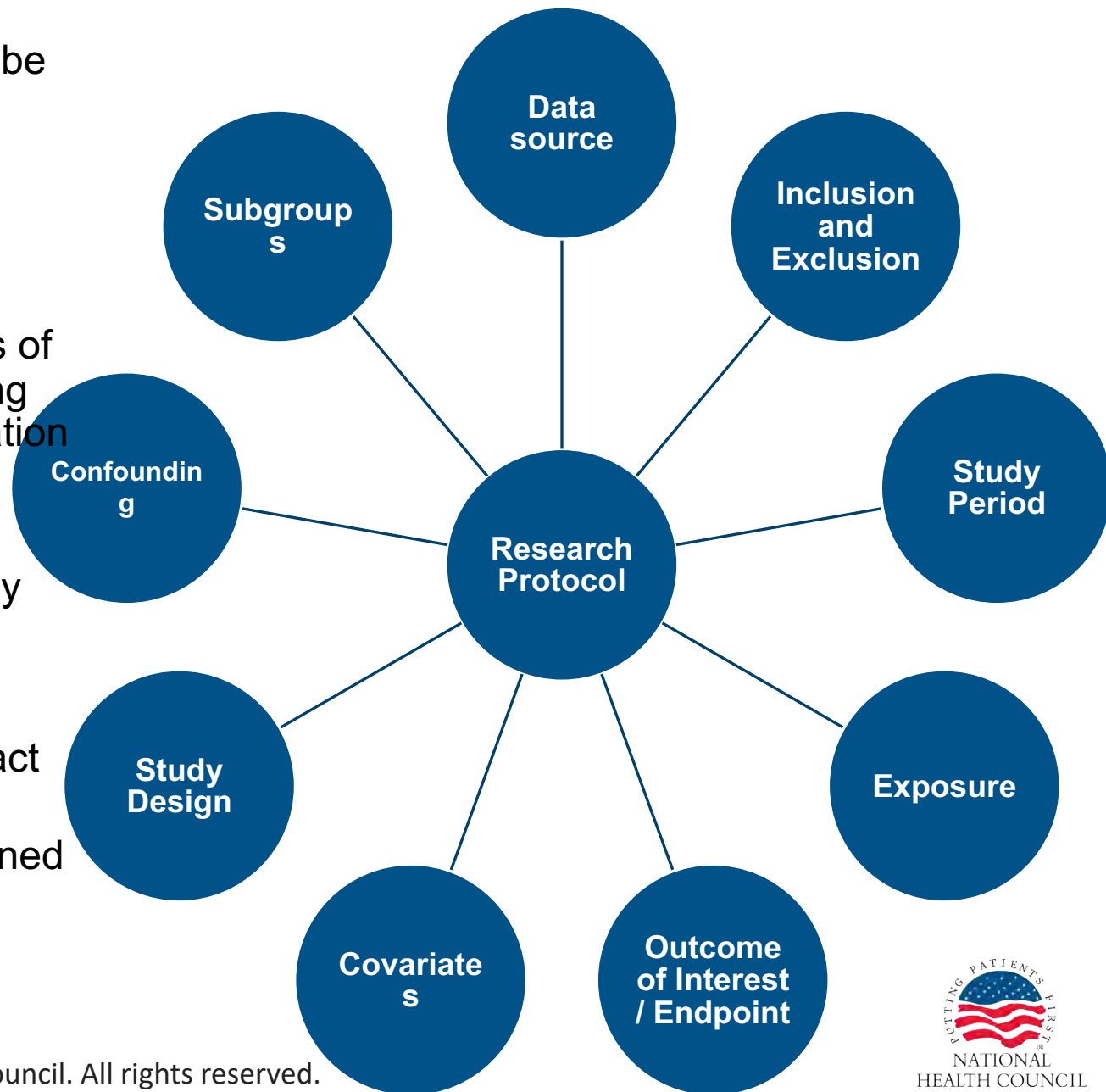
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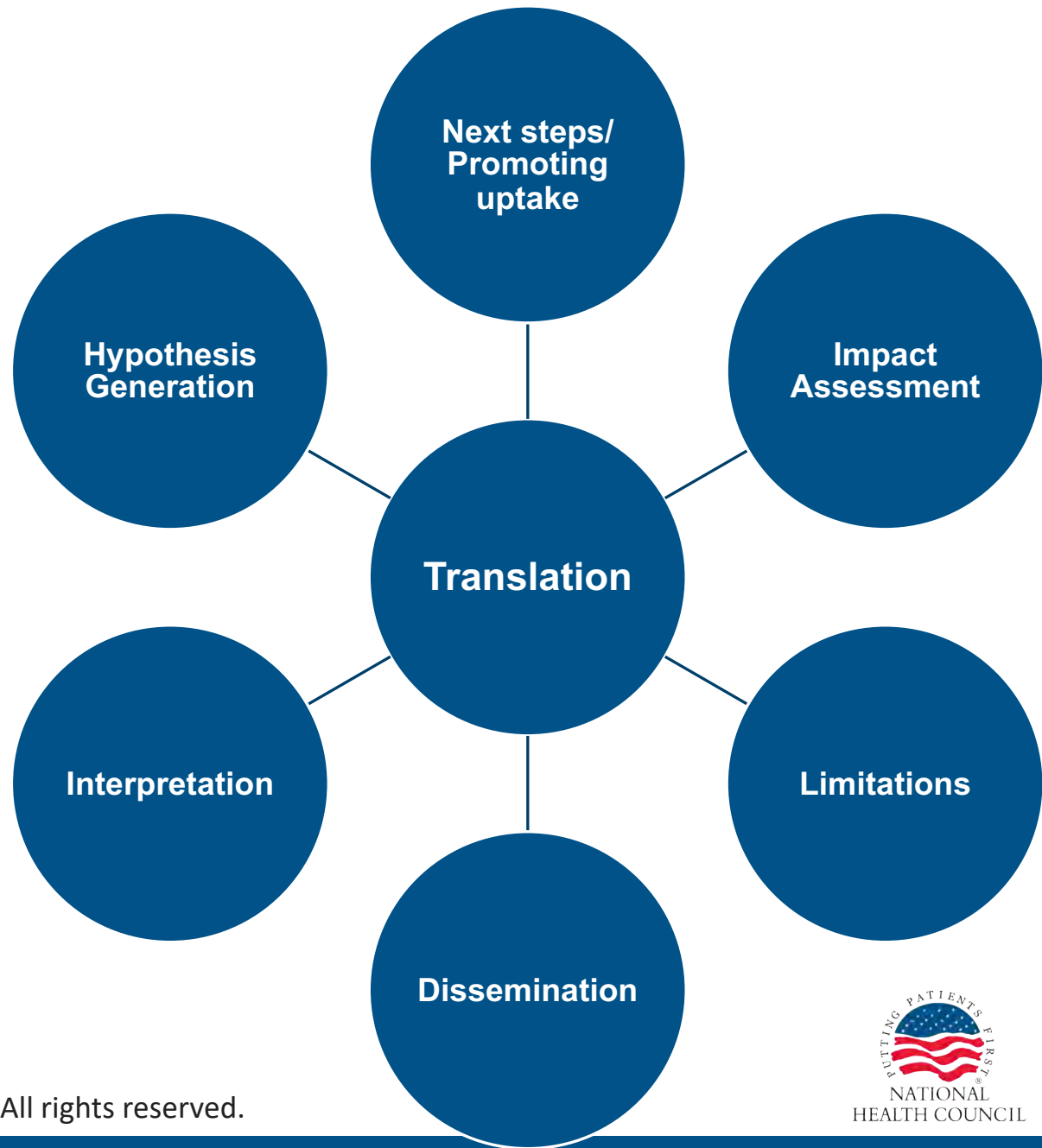
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