

STEP: Design and Logistics Overview

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STEP MPI and Protocol PI, on behalf of the STEP Executive Committee

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Disclosures

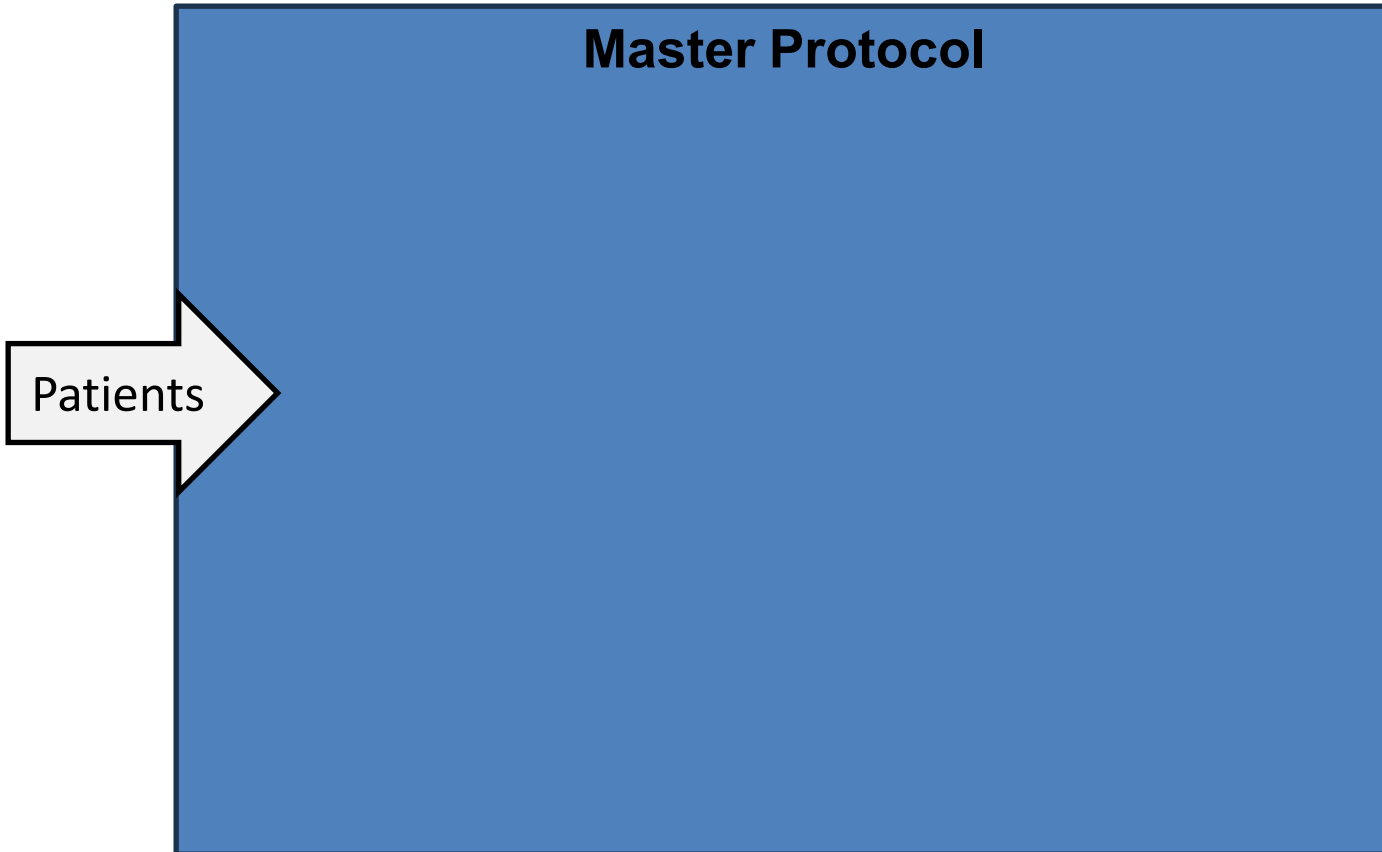
Affiliation/Financial Relationship	Organization/Company
Grant/Research Support	<ul style="list-style-type: none"><li data-bbox="1289 425 2066 586">• <u>NIH</u> (UG3/UH3NS125023 , U24NS107241, 1OT2NS129366, K23NS113858)<li data-bbox="1289 605 1951 654">• <u>PCORI</u> (AD-2022C1-25624)
Consulting Fees/Honoraria	<ul style="list-style-type: none"><li data-bbox="1289 719 2040 819">• RAPID AI/iSchemiaView, AbbVie, SilverCreek Pharma, AAN
Other Financial Benefit	<ul style="list-style-type: none"><li data-bbox="1289 872 2109 972">• American Heart Association (compensation for editorial services)
Other Non-financial Disclosure	<ul style="list-style-type: none"><li data-bbox="1289 1025 1900 1066">• Translational Sciences Inc

STEP Design



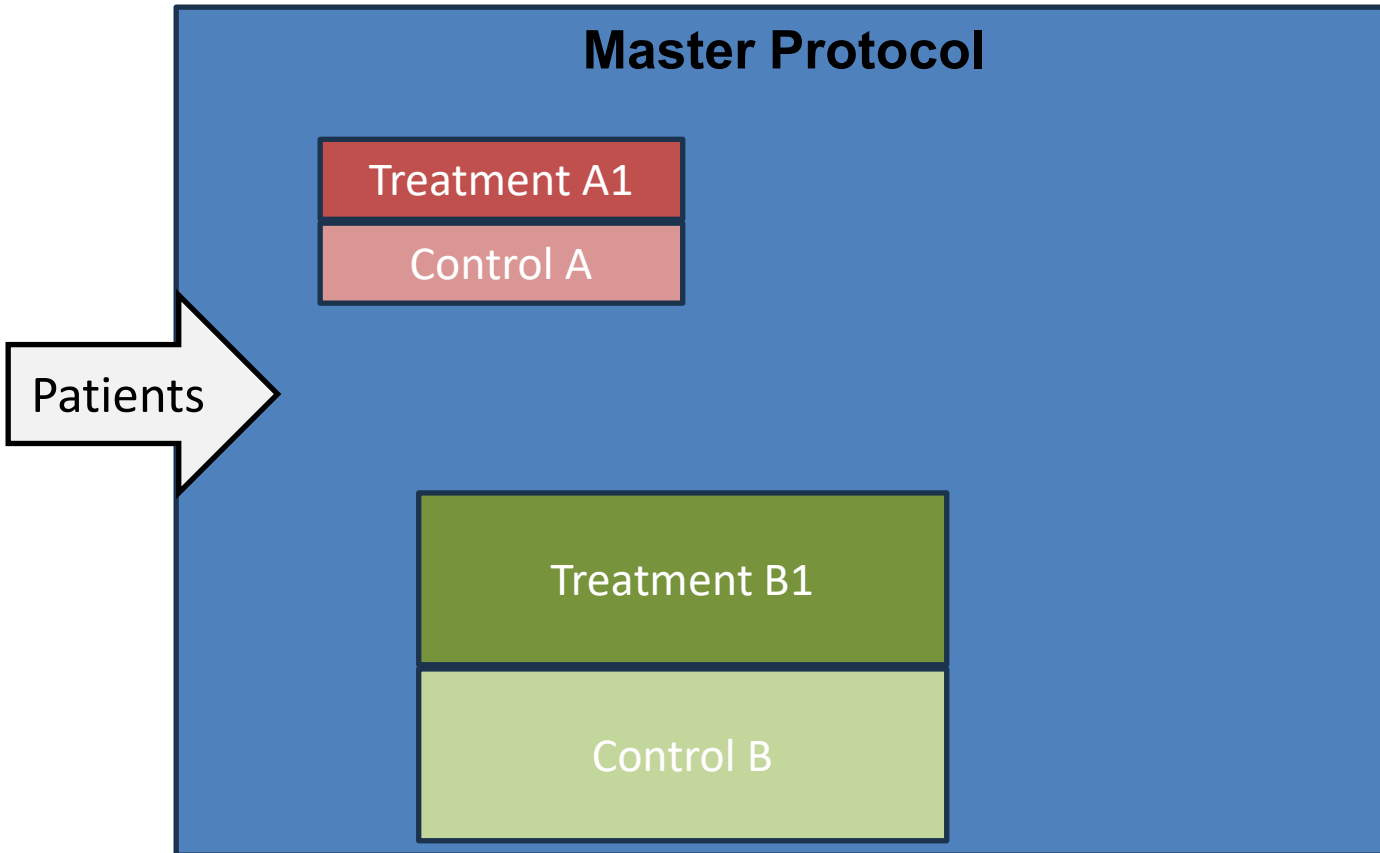
- Randomized Multifactorial Adaptive Platform (REMAP design)
- 38 sites across the US
- Leverages existing registries for data collection
 - AHA Get with the Guidelines
 - NVQI-QOD

STEP- Master Protocol



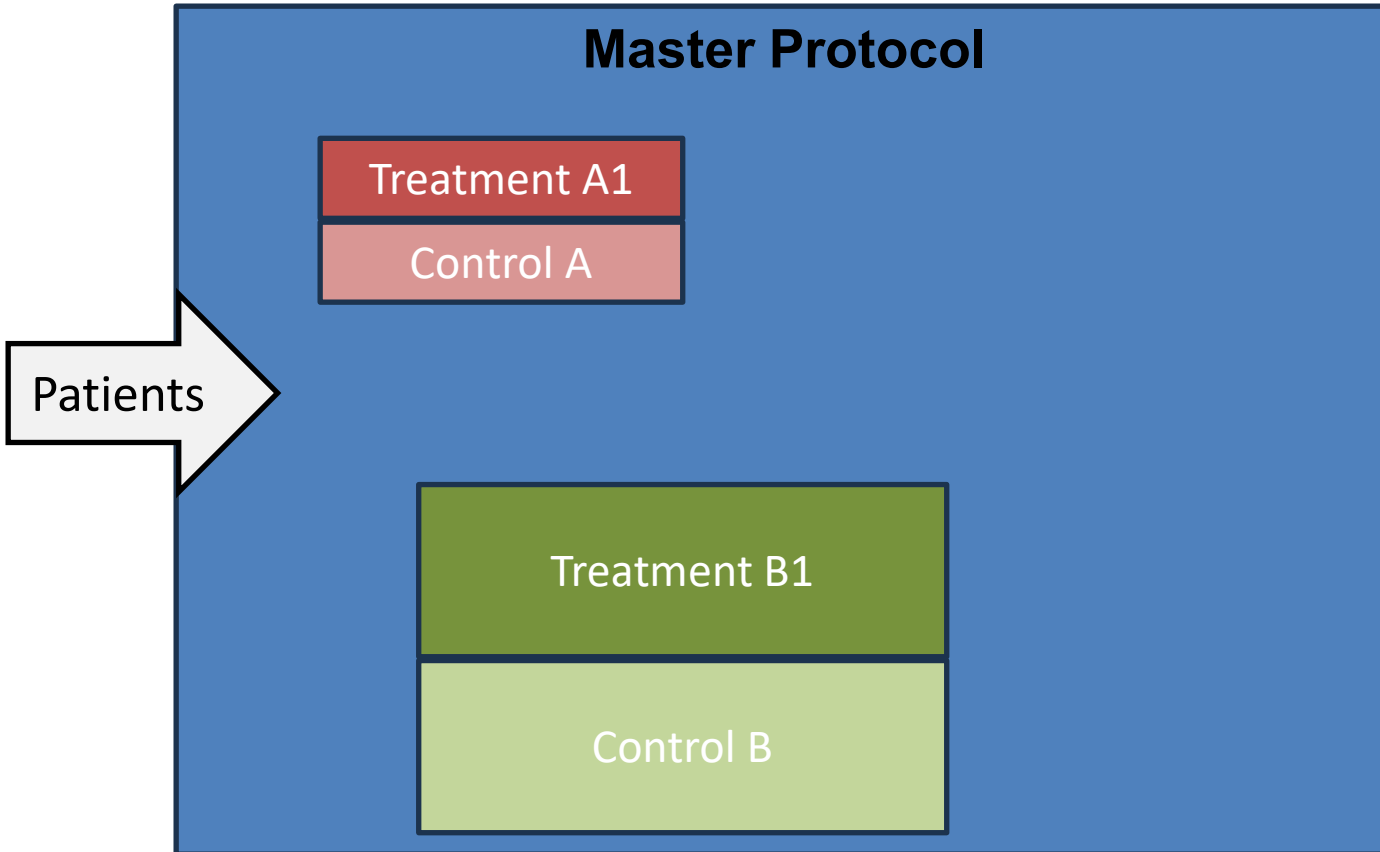
- Defines the largest set of Inclusion/Exclusion Criteria to be studied
 - ✓ Acute ischemic stroke patients
 - ✓ Intracranial large or medium vessel occlusion
- Broadly defines overall study terminology and research procedures
 - ✓ STEP primary outcome is 90-day mRS (using utility weighted approach)
- Specifies a single underlying statistical model

STEP- Domains (studies of interventions)



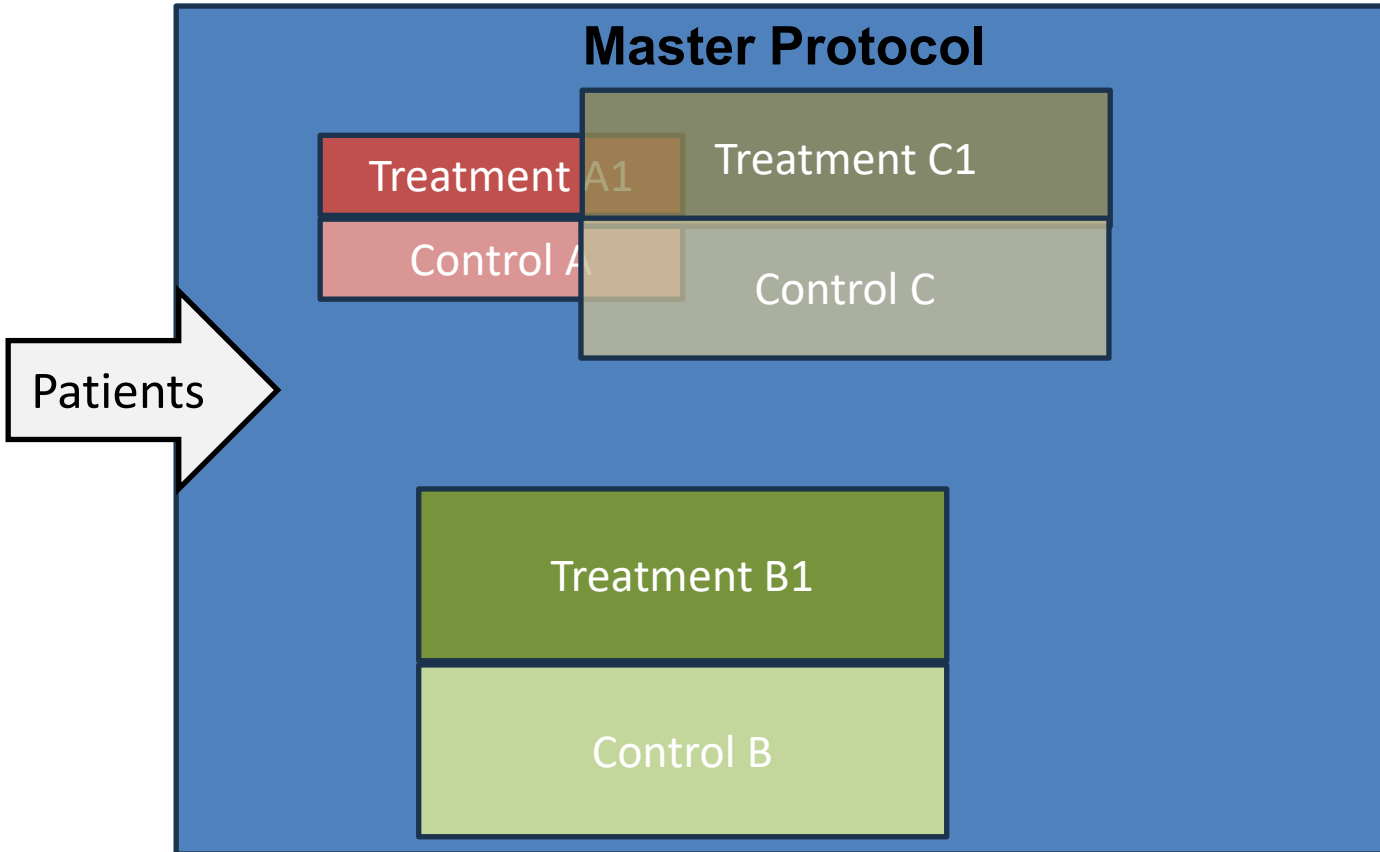
- Studies of **mutually exclusive** interventions
 - ✓ Domain A- EVT vs MM
 - NIHSS<6
 - Medium/distal vessel occlusions
 - ✓ (Hypothetical) Domain B- Neuroprotectant 1 vs Neuroprotectant 2 vs control
 - ✓ (Hypothetical) Domain B- Adjunctive therapy 1 vs control
- Patients can be randomized within multiple domains (**multifactorial**)

STEP- Domains specific appendices



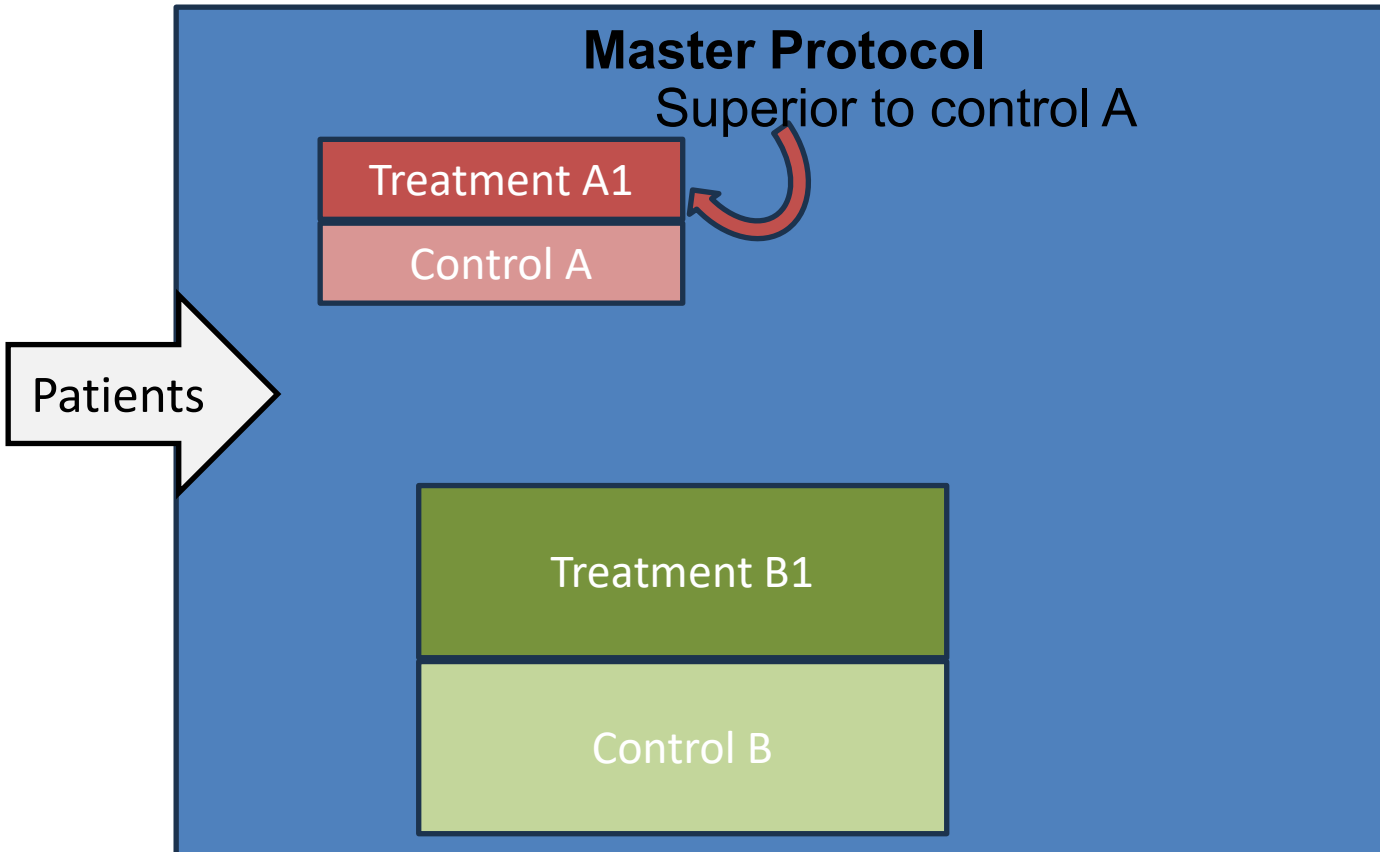
- Defines a I/E criteria for domain-eligible patients
- Details the type/delivery of intervention(s)
- Detailed specifics
 - ✓ Randomization/ adaptations
 - ✓ Analysis methods
 - ✓ Additional research procedures
 - ✓ co-enrollment

STEP- Domains (studies of interventions)



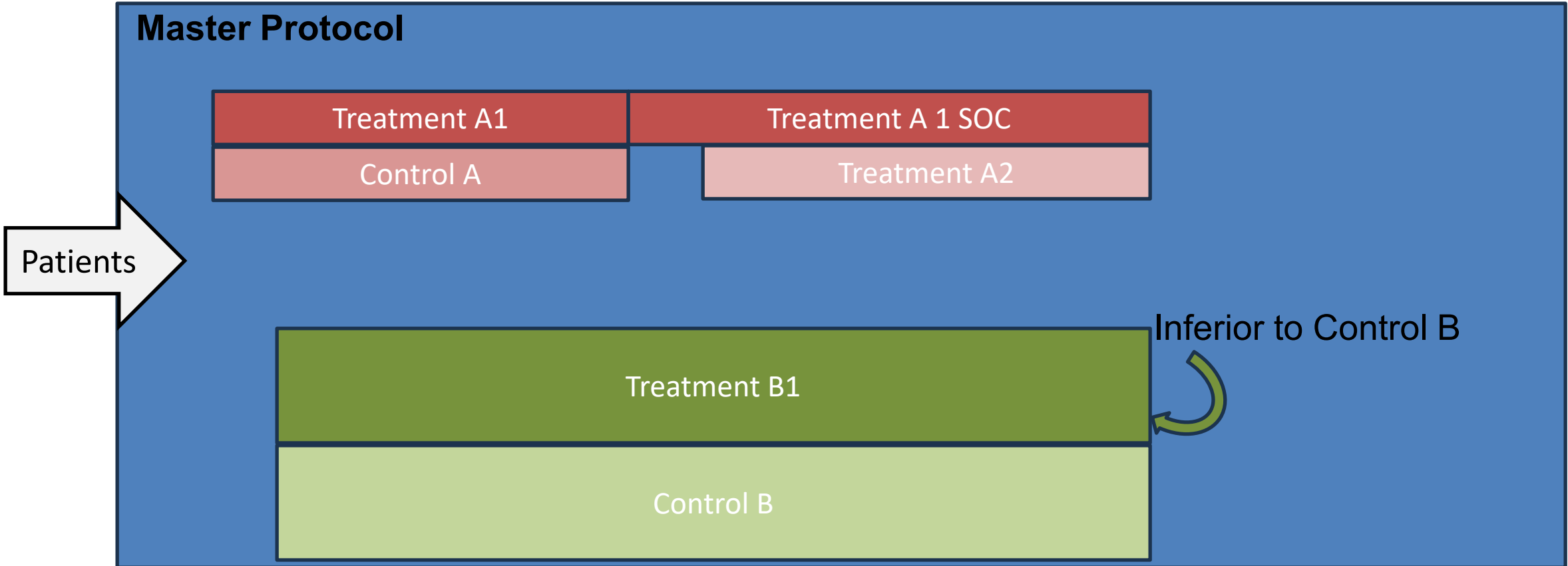
- Treatment within the domains are mutually exclusive but the patient population can overlap between two domains
- Patients can be randomized within multiple domains (**multifactorial**)

STEP enduring platform- Decisions

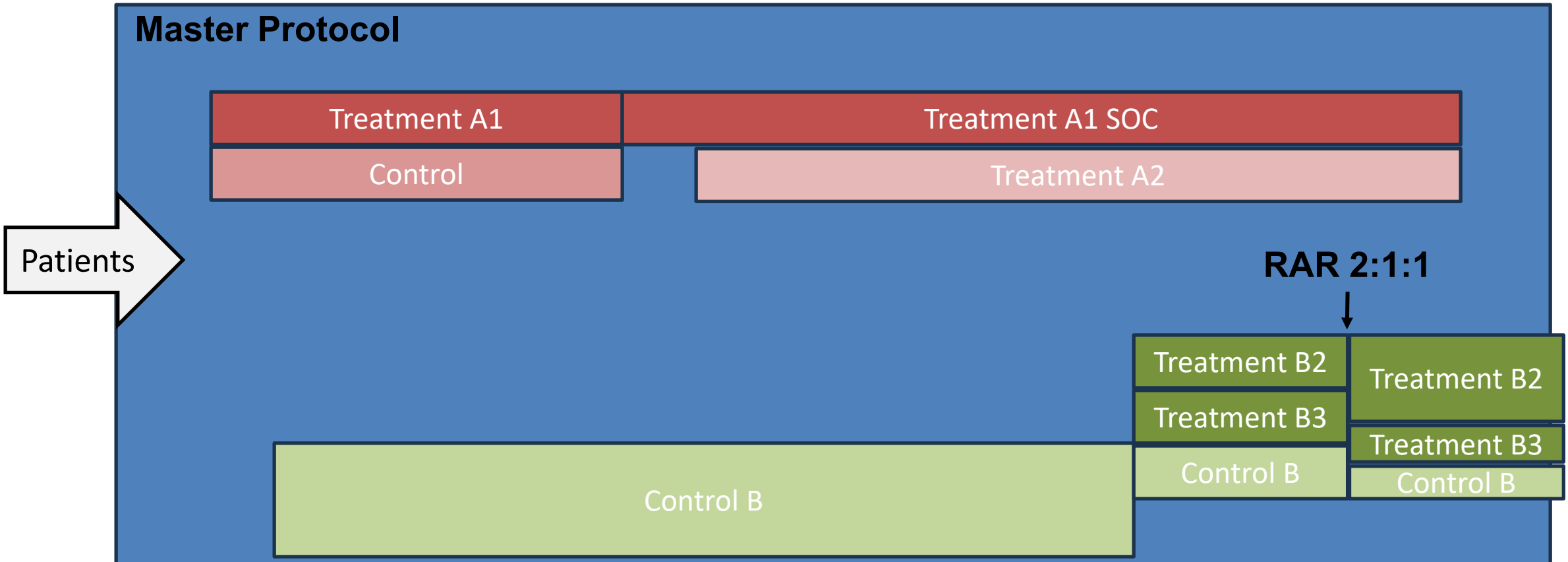


- Following types of decisions can be made for an entire domain or particular domain arm (s) or pre-defined subset of patient population (strata)
 - ✓ Superior
 - ✓ Inferior
 - ✓ Futile
 - ✓ Equivalent
- Decisions are based on statistical triggers
 - ✓ Based on pre-defined analysis frequency
 - ✓ Using platform statistical model

STEP enduring platform- Therapy domains can be perpetually added



STEP employs response adaptive randomization (RAR)



STEP Statistical Model



- **Single inferential model:** model the primary outcome as a function of each randomized treatment from each domain

$$Y = [\text{covariates}] + [\text{intervention effects}] + [\text{intervention} \times \text{stratum}] \\ + [\text{intervention} \times \text{intervention}] + [\text{error}]$$

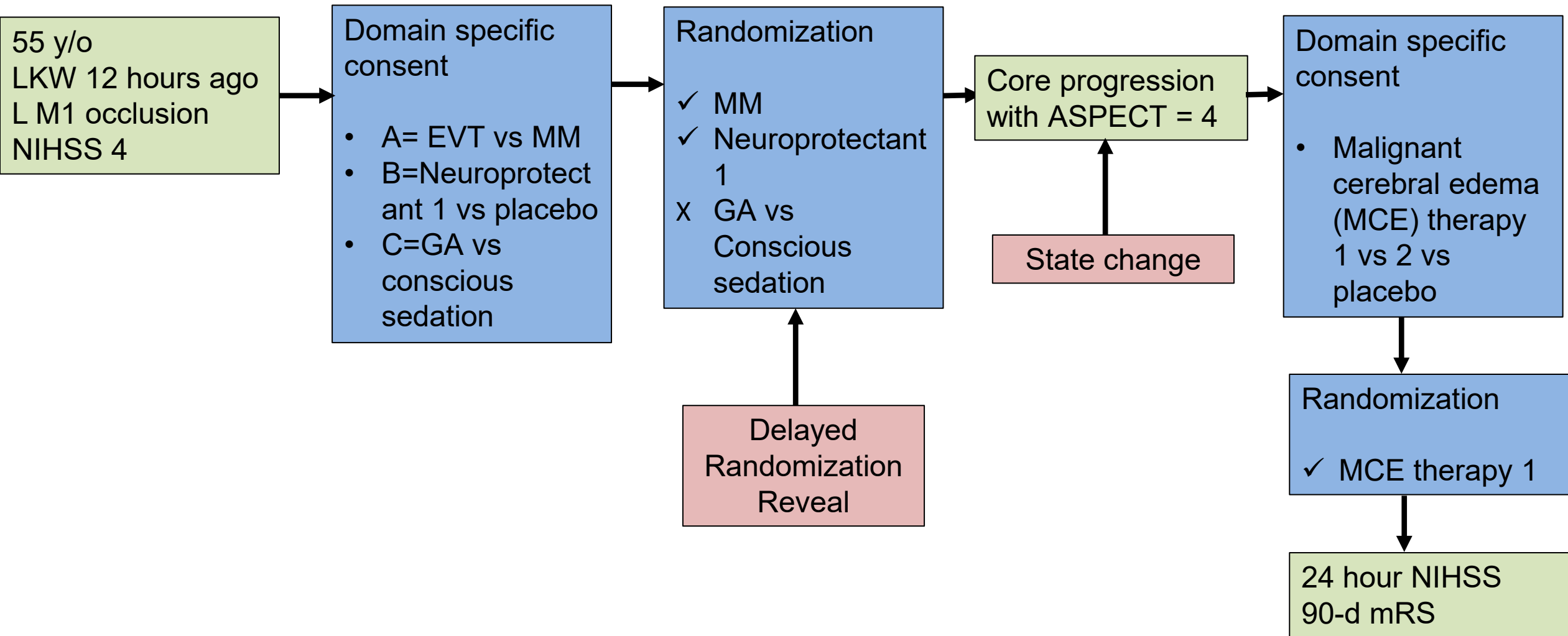
- Can address across domain interactions

STEP- Consent Procedures

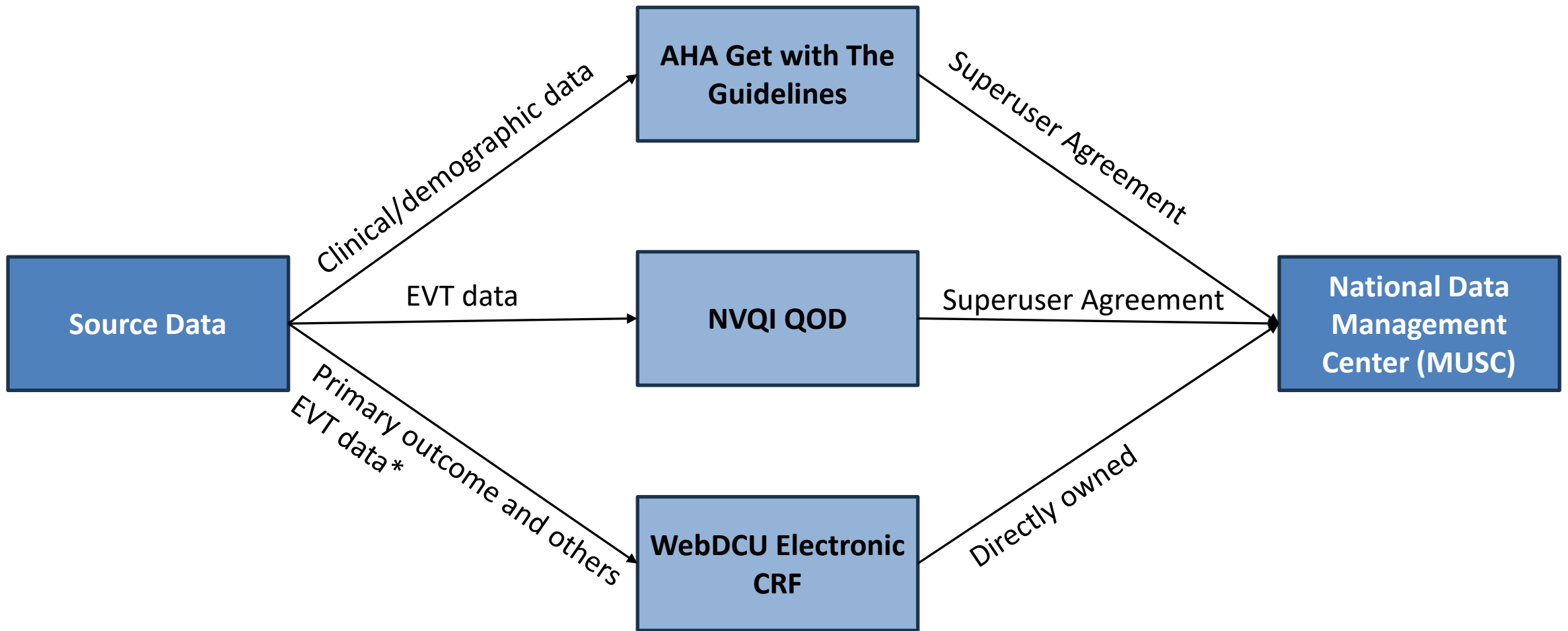


- Domain specific consent forms:
 - Electronic consent is required (unless participant or LAR prefers paper consent)
 - Remote consent is encouraged for transfer patients
 - Domain specific consents are shown according to specific inclusion/exclusion criteria for given domains
 - As a participant becomes eligible for more domains, consent forms specific to those can be presented
- Master protocol participant information sheet
 - Two- page sheet explaining the concept of platform in lay language
 - Does not need to be signed

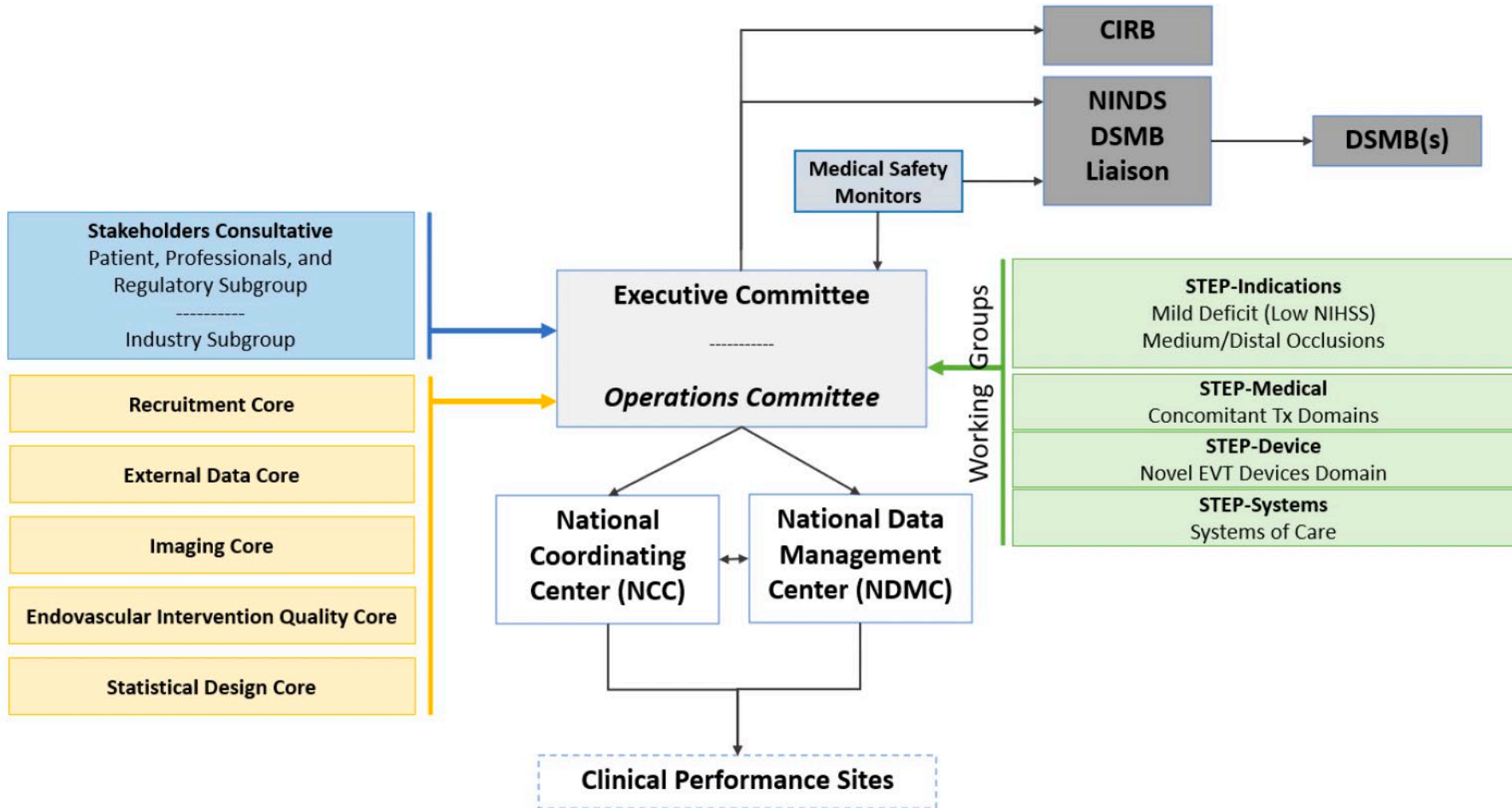
Enrollment Example-1



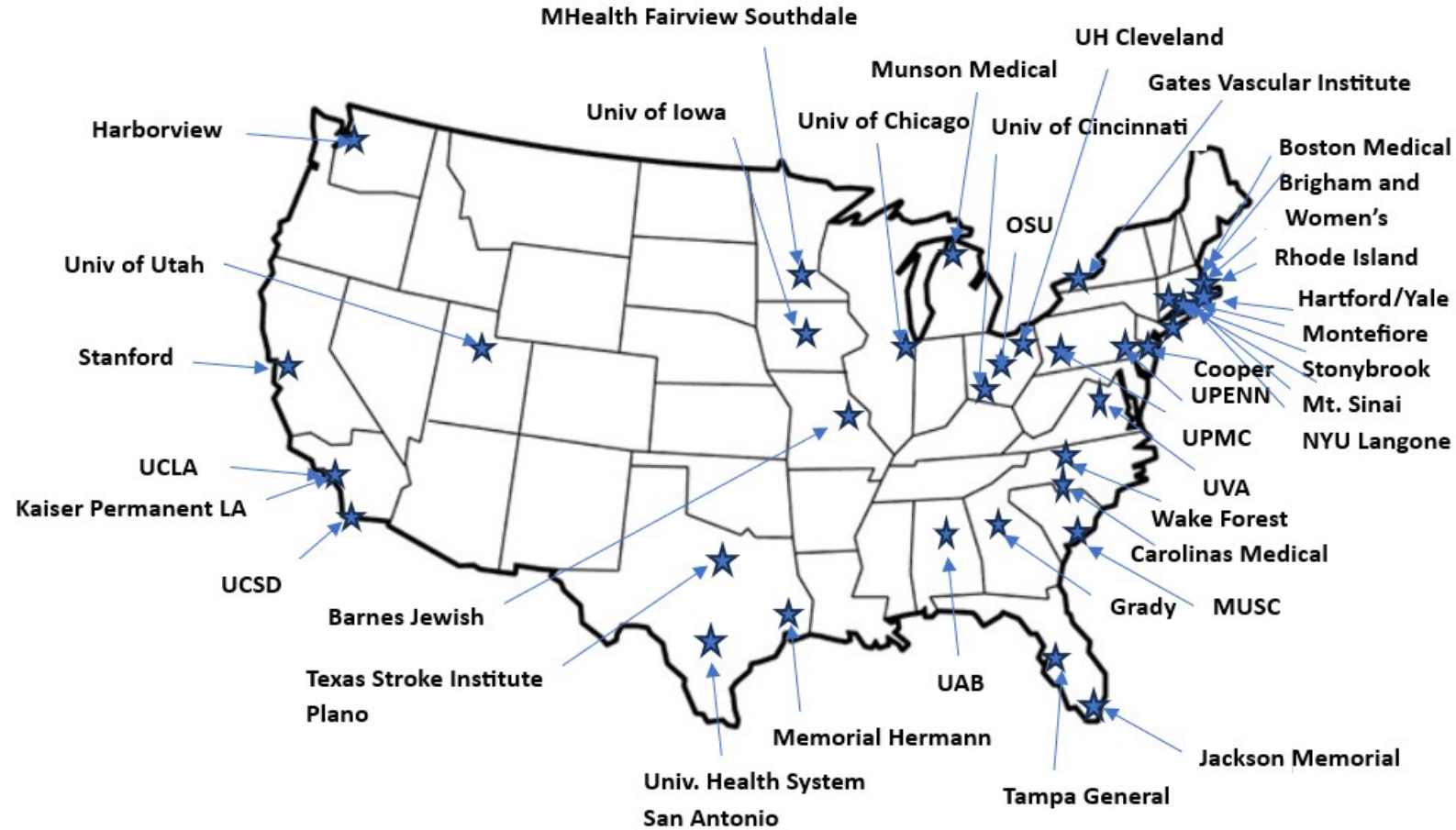
STEP Data Transfer Procedures



STEP Community - Organization



STEP Community- Participating Sites



Thank you!

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