

Reporting of Stroke Outcomes in Cardiovascular Randomized Controlled Trials

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Background

- Stroke is not consistently defined in clinical practice, clinical research and public health
- Advances in technology have prompted the revision of the definition of stroke in 2013 by the AHA/ASA to include imaging modalities
- More patient-centered outcomes (eg. disabling strokes) and less patient-centered outcomes (eg. silent strokes) may be compiled together into an outcome of "stroke"
- In order to support patients, clinicians, researchers and policy makers in their interpretation and application of the cardiovascular literature, clinical outcomes need to be transparently and unambiguously defined in RCTs
- ACC, AHA, FDA and SCTI have collaborated to develop 2014 clinical data standards for important cardiovascular endpoint events in clinical trials
 - Stroke is defined as "an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction"
 - In contrast to TIA, stroke is defined on the basis of presence of acute infarction seen on imaging or by persistence of symptoms
 - Incidence of new stroke, type of stroke and severity of stroke (modified Rankin Scale is recommended as the measure of disability) should be reported in clinical trials

Objectives

- To systematically evaluate in a sample of large RCTs
 - How many trials define stroke and disabling stroke
 - Where the definition of stroke is found
 - How stroke and disabling stroke are defined

Methods

Inclusion Criteria

- RCTs (n ≥ 1000) published in N Engl J Med, JAMA, Lancet, Ann Intern Med, PLoS Med, BMJ, Circulation, J Am Coll Cardiol, Neurology, Stroke or Eur Heart J identified on PubMed that reported "stroke" as an outcome at the abstract level

Exclusion Criteria

- Substudies unless original publication not captured in screening process
- Studies where both arms were non-drug

Data Extraction

- Systematically searched for definition of stroke and stopped when definition found
- Data collected regarding presence of components of stroke definition based on 2014 AHA/ACC guidance

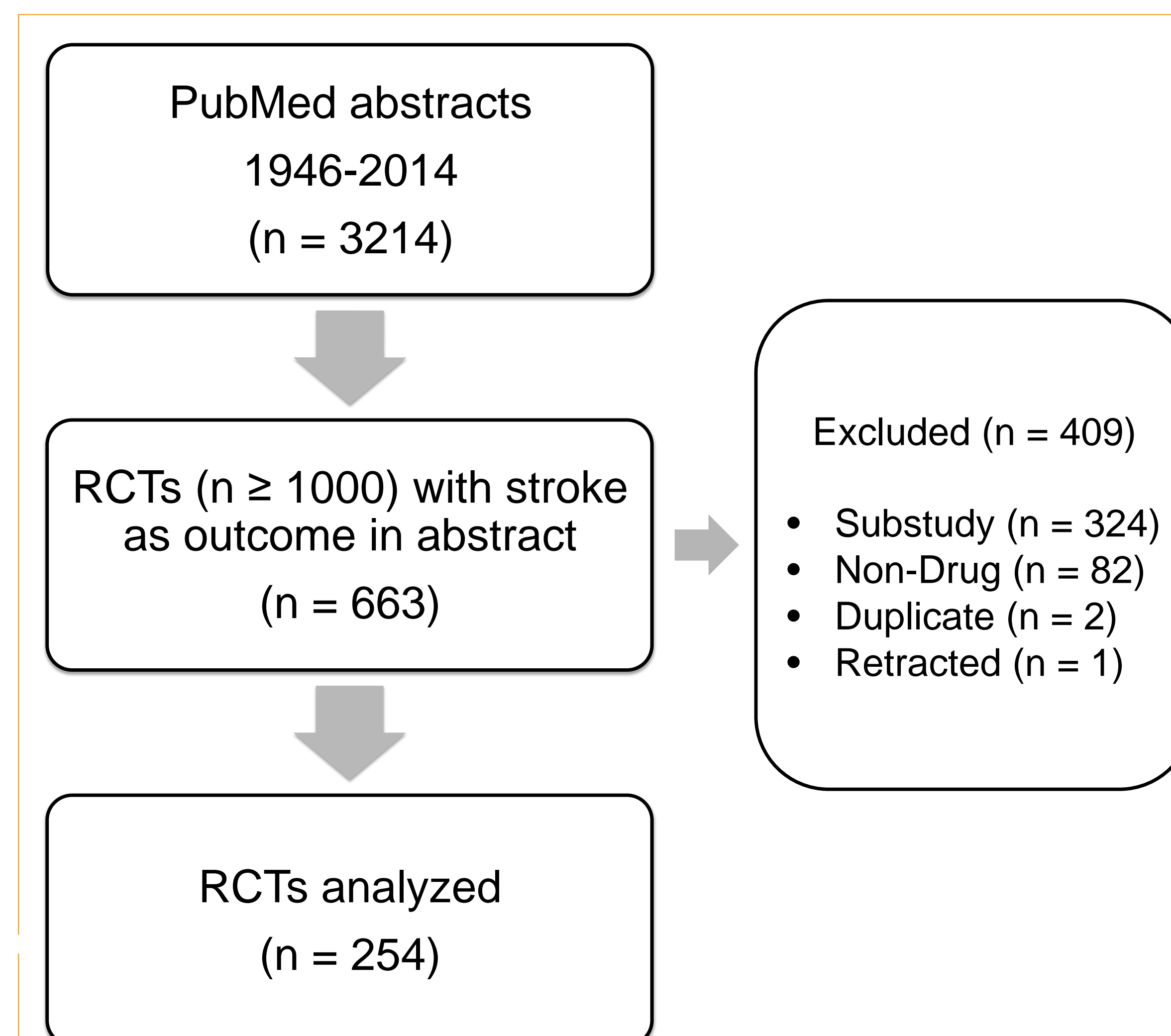


Figure 1. Study flow diagram.

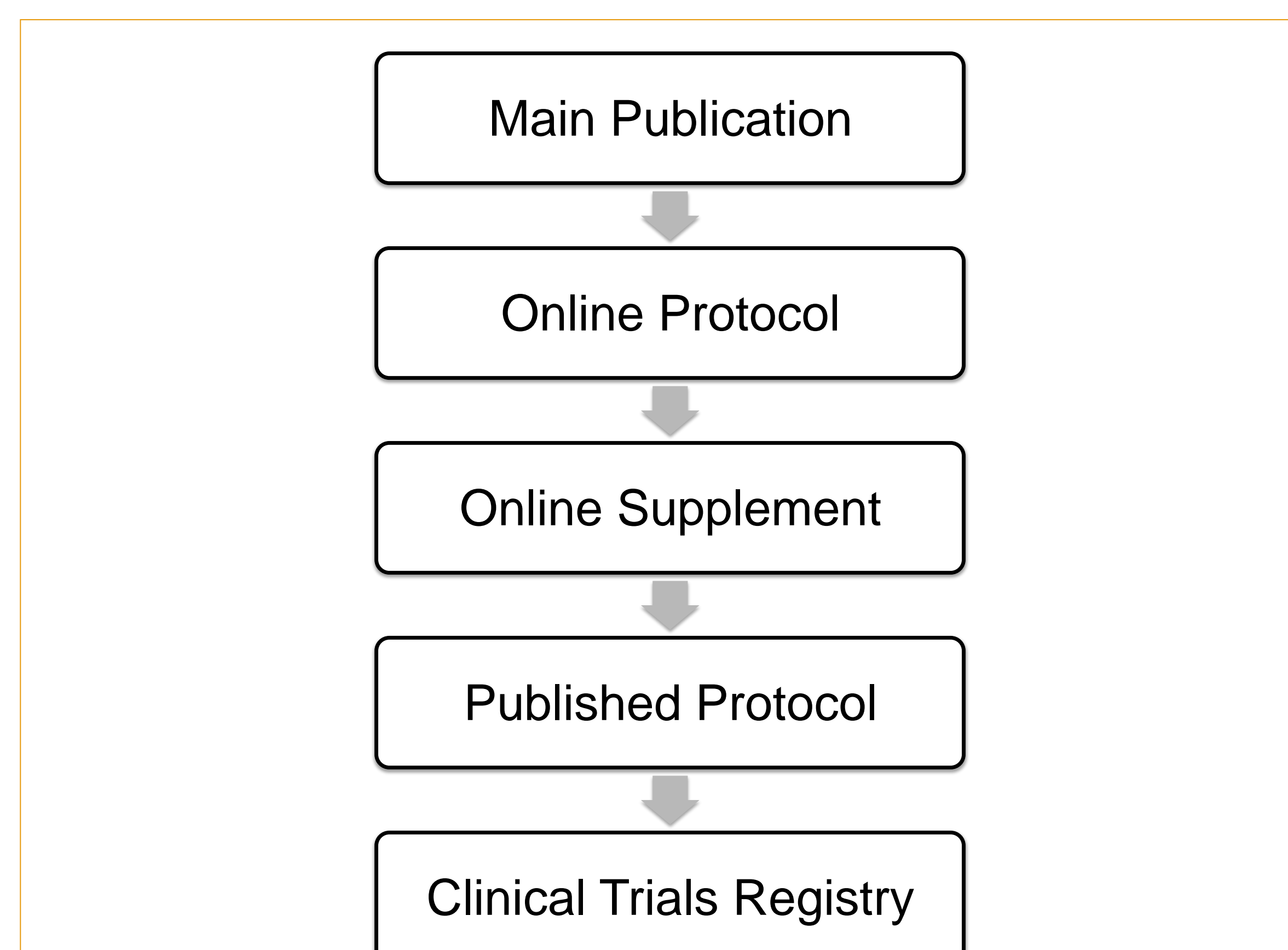


Figure 2. Data extraction process.

Abbreviations

- AHA: American Heart Association
- ASA: American Stroke Association
- ACC: American College of Cardiology
- FDA: U.S. Food and Drug Administration
- SCTI: Standardized Data Collection for Cardiovascular Trials Initiative
- TIA: Transient Ischemic Attack
- RCT: Randomized Controlled Trial

Results

Definition (n = 254)	
Stroke	148 (58%)
Disabling Stroke	42 (17%)

Table 1. Proportion of trials with definition of stroke and disabling stroke.

Components of Stroke Definition (n = 148)		
Clinical	Acute	81 (55%)
	Neurological	128 (86%)
	Symptoms	138 (93%)
	Persistence of Symptoms	126 (85%)
Technology	Duration of Persistence ≥ 24 hours	120 (81%)
	Imaging	108 (73%)
	Brain	21 (14%)
	Spinal Cord	1 (0.7%)
Location	Retinal Vascular injury	5 (3%)
	Vascular	51 (34%)
	Ischemic	91 (61%)
Type	Hemorrhagic	83 (56%)
	Undetermined	53 (36%)

Location of Stroke Definition (n = 148)	
Main Publication	94 (64%)
Protocol and/or Supplement	54 (36%)
Stroke Disability Scale (n = 42)	
Any Scale	37 (88%)
Modified Rankin Scale	28 (67%)

Table 2. Proportion of trials with components of stroke definition, location of stroke definition, and proportion of trials using a stroke disability scale.

Conclusion

- 42% of cardiovascular RCTs reporting stroke as an outcome do not provide a definition of this outcome in the main publication, protocol, supplement or clinical trials registry
- 85% of RCTs providing a definition for the outcome of stroke define persistence of symptoms but only 17% of all RCTs include a definition for disabling stroke
- 73% of RCTs report using medical imaging in the diagnostic process but few specify the location of the vascular injury
- Only 64% of RCTs providing a definition for the outcome of stroke provide the definition in the main publication. Therefore, users of cardiovascular literature would frequently need to search the protocol and/or supplement to identify the definition