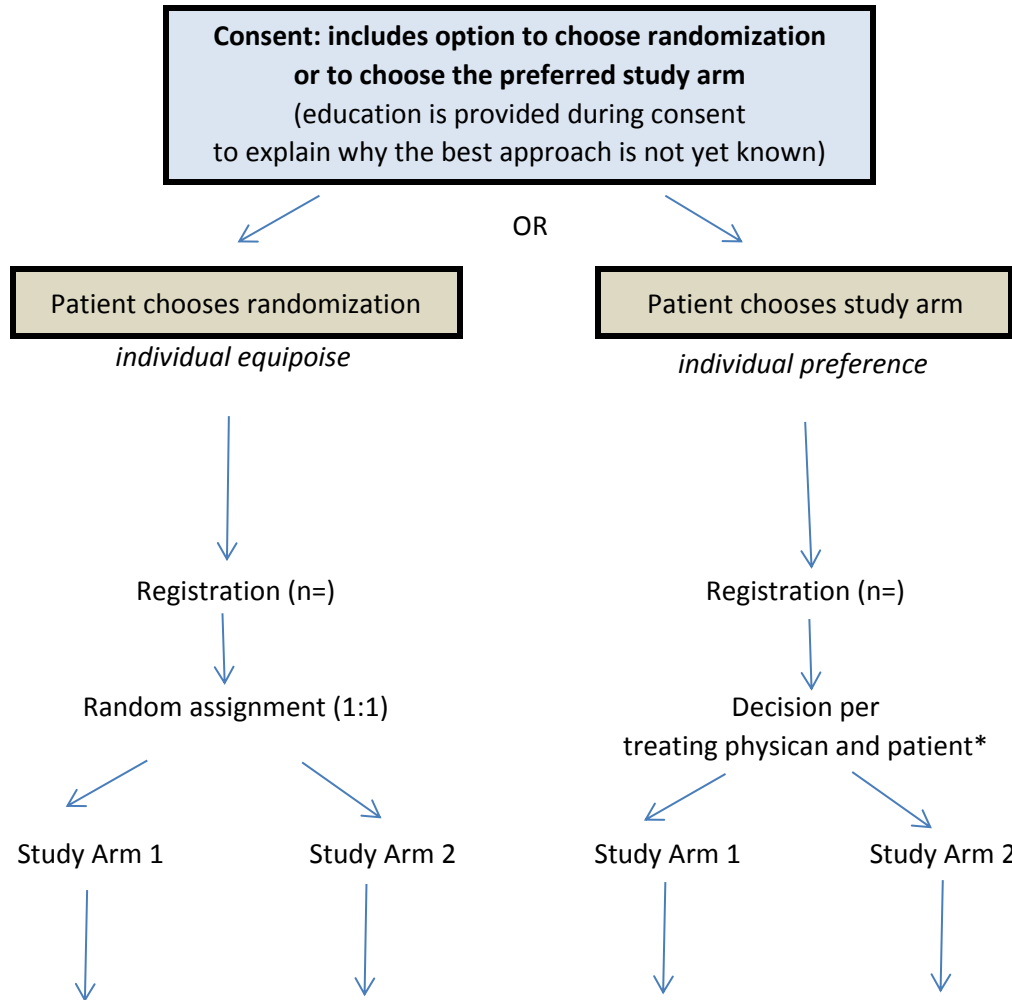


Observation-enriched Randomized Controlled Trial (ORCT)

a hybrid allocation study design

to consider when the gold-standard RCT is not feasible to get done



Propensity scoring can help correct for bias in observation arms

Study arms can be closed to achieve minimum random allocations or balance in observation arms

* Referring centers can be randomized - or selected to correct for known institutional preferences

Consider when comparing approaches with very different risks

Consider when either or both treatments can be used off study

Consider when biomarker discovery is primary endpoint

... and heterogenous disease biology predicting outcomes is not known

Will foster efficient accrual in large trials - consent decisions can be captured and evaluated

Mitigates selection bias associated with "volunteering to be randomized"

Observation arms having same eligibility and response assessment - thus are superior to historical controls

ORCT is superior to single-arm study or RCT that's not feasible to get done

Comparison of Observation and Randomized cohorts tests the validity of Observation data

ORCT design maximizes respect for persons