

Statistical Analysis Plan Checklist for Addressing COVID-19 Impacts

Since early 2020, the COVID-19 public health emergency has compelled clinical research teams to postpone recruitment, alter methods of participant engagement, and modify tools for research assessment and intervention delivery. The NIH Health Care Systems Research Collaboratory has sought to navigate the impacts of study disruption on pragmatic clinical trials embedded in healthcare systems and to identify strategies for maintaining patient and staff safety while ensuring rigorous research design and conduct.

The checklist below links major elements of study conduct to the specification or modification of statistical analysis plans to address unique challenges associated with data collection, research measurement, and analysis in pragmatic clinical trials. The checklist uses the Population, Intervention, Comparison, Outcome, Timing, Setting (PICOTS) framework for summarizing research questions to identify impacts on study conduct that should be documented, measured, analyzed, and reported.

Table 1. COVID-19 Statistical Analysis Plan Checklist

PICOTS Element	Document and Measure	Analyze and Report
Population	<input type="checkbox"/> Measure changes to participants' demographic and clinical characteristics	<input type="checkbox"/> Compare participants' baseline characteristics over time (for example, before and after March 2020)
	<input type="checkbox"/> Measure changes to participants' access	<input type="checkbox"/> Compare participants' characteristics over and attitudes (for example, see time periods defined by local COVID-19 Coronavirus Impact Scale) status or impacts on research conduct
	<input type="checkbox"/> Evaluate COVID-19-related methods for electronic phenotyping	
Intervention	<input type="checkbox"/> Document modifications to the intervention to ensure the safety of patients and providers	<input type="checkbox"/> Compare engagement in intervention components over time periods
	<input type="checkbox"/> Document and measure changes to methods to communicate and deliver the intervention	<input type="checkbox"/> Consider modifying the primary analysis to adjust (stratify) for COVID-19 phases

COVID-19 SAP Checklist

Document and measure changes to any components or mechanisms associated with the intervention

Consider sensitivity analyses that restrict to periods of time based on COVID-19 status

Consider subgroup (interaction) analysis of heterogeneity of treatment effect across COVID-19 time periods due to changes in the intervention (or other factors)

Consider time-specific mediation analysis to evaluate putative mechanisms across COVID-19 time periods

Comparison

Document modifications to the comparison to ensure the safety of patients and providers

Compare engagement in the comparison (such as usual care) over time periods

Measure trends in concomitant care over time

Clarify the estimand of interest, typically the average treatment effect that averages over explicit participant and time characteristics while potentially controlling certain factors

Consider subgroup (interaction) analysis of heterogeneity of treatment effect across COVID-19 time periods due to changes in usual care (or other factors)

Report the consequence of COVID-19 impacts that are specific to the study design (for example, parallel randomized trials will be affected differently than crossover or stepped-wedge designs)

Outcome

Document and measure changes in how clinical assessments and patient-reported outcomes are obtained

Report psychometric properties of any modified measures

Measure impacts of COVID-related distress on patient-reported outcomes

Consider subgroup analyses based on patient-reported characteristics at baseline that are predictive of outcomes or COVID-19 susceptibility

Describe temporal trends in patient reported outcomes

Evaluate patterns and correlates of missing data over time to assess differential nonresponse

Timing

Document COVID-19 status at the regional level over time

Consider effect modification with proximal measures of COVID-19 impact (patient level, clinical level)

COVID-19 SAP Checklist

	<input type="checkbox"/> Document COVID status at the clinic level	<input type="checkbox"/> Describe longitudinal trajectories in participant outcomes across treatment groups and COVID-19 time periods
	<input type="checkbox"/> Measure participant-level impacts of COVID-19 over time	
	<input type="checkbox"/> Consider evaluating participant outcomes at longer (or shorter) lags to determine potential impacts on response trajectories	
Setting	<input type="checkbox"/> Document changes to the research setting (or modality) for both intervention delivery and participant assessment	<input type="checkbox"/> Describe differences in the intervention, the comparison, and concomitant care across research settings
		<input type="checkbox"/> Describe differences in outcomes across research settings