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Comparing Analysis Method Implementations in Software (CAMIS): An open source repository to document differences in statistical methodology software

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CAMIS Working Group

Background:

Statisticians and programmers working in multiple software systems (e.g. SAS, R, Python), will have found differences in analysis results that warrant further exploration and justification. Whilst some industries, may accept results not being the same as long as they are "close" -- the more highly regulated medical research industry generally uses double programming to validate results. This approach requires an identical match in results. This can be very challenging and highly time consuming to investigate and justify any differences, particularly when accompanying documentation doesn't fully explain the approach used by the software.

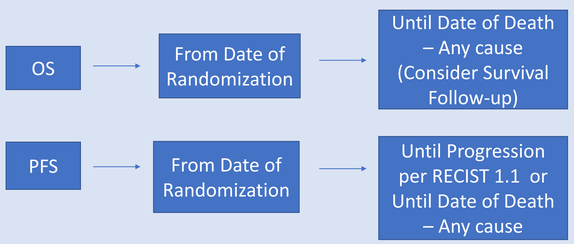
The CAMIS project aims to provide a repository of information explaining why you may be observing differences when working in SAS and open source languages.

This poster will highlight the latest status of the PHUSE CAMIS project including our finalized white paper and growing repository, with the aim of encouraging further contributions from the wider PHUSE community.

This will be an update on our progress in collaboration with FDA and PHUSE community, **CAMIS-ONCO** subgroup started in September 2023 with focus on Oncology endpoint analysis, validation in multi-programming world.

FDA on Oncology Clinical trial Endpoints:

FDA has standardized **Oncology trial endpoints definitions**, including study design recommendations, highlighting advantages and disadvantages across pharmaceutical industry for approvals. These definitions e.g.: **Overall Survival (OS), Progression Free Survival (PFS)** are standardized to an extent that now can be considered as **"Algorithms"** of oncology efficacy programming and statistics. In many trials, these are primary efficacy endpoints and play a crucial role in approval of drugs.

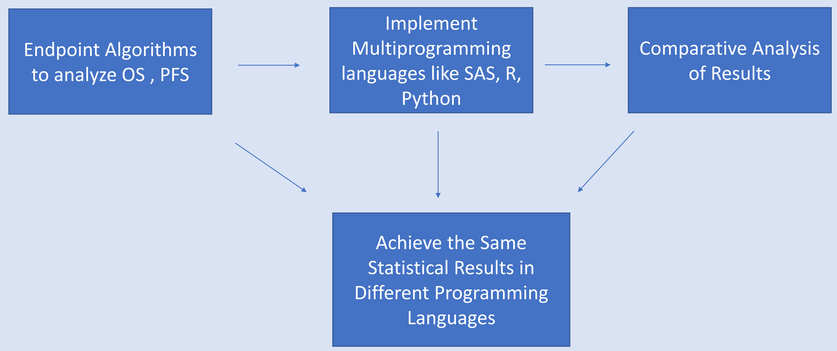


Download the FDA's recommendations for your Study Protocol, SAP, and Dataset Specifications

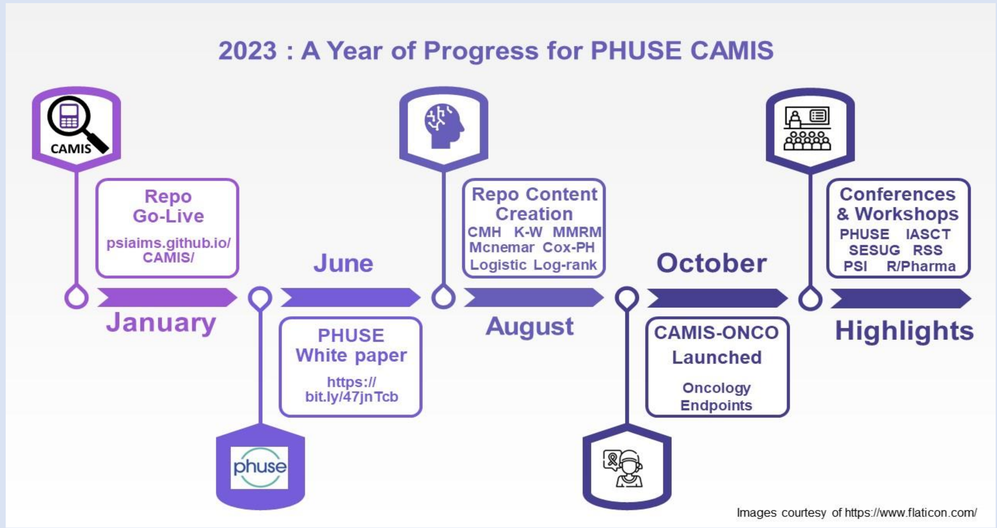
Other than **Deaths** due to any reason on trial, including **Grade 5 Adverse events** due to drug, **Progression of Disease (PD)** becomes an important indicator to be evaluated, to perform comparison between two treatment arms, and establish statistical significance. The Progression is defined by **RECIST 1.1** ("Algorithm"), assessed by Independent Review Committee (IRC) or Investigator . The measure of interest being **Hazards ratio of OS or PFS.**

The **standardized derivations or algorithms** recommendation to analyze endpoints opens an opportunity to implement different programming languages in analysis or validation of results.

CAMIS-ONCO Flow Chart:



CAMIS: Comparing Analysis Method Implementations in Software



CHEAT SHEET:

Endpoint	SAS	R	Python
Generate Hazard ratio from Cox model and confidence interval from log rank test for OS/PFS analysis on Full Analysis set or Intent-to-treat population between TRTA and TRTB – stratified by Region { Discuss using efron method }	data adtte; set adam.adtte; where paramcd = 'OS' 'PFS'; run; proc phreg data = adtte; class trt; model aval*censor(0) = trt/rl ties = efron; strata region; run;	adtte <- subset(adam.adtte, paramcd == 'OS') or 'PFS' fit.cox <- coxph(Surv(Aval, censor) ~ trt + strata(region), data = adtte)	adtte = adam.adtte[adam.adtte['paramcd'] == 'OS'] or 'PFS' cph.fit(adtte, duration_col = 'Aval', event_col = 'censor', strata=['region'])
- Confidence Interval { Use log-log transformation }	proc lifetest data = adtte; time aval*censor(0); strata region/group = trt; run;	fit.km<- survfit(Surv(Aval, censor) ~ trt + strata(region), conf.type = "log-log", data = adtte)	confidence_interval = kmf.confidence_interval_() {Default option is log}
Test ORR between TRTA and TRTB on Full Analysis set {odds ratio from logistic regression model}	Proc genmod data = adrs; class trt ; model aval = trt /dist = binomal link = logit lrci; lsmeans trt/pdiff cl exp means; run;	model <- glm(aval~ trt, data = adrs, family = binomial) exp(coef(model))#odds ratio exp(confint(model))#C I	# Logistic regression model X = df['trt'] #independent variable Y=df['aval'] # dependent variable X = sm.add_constant(X)#intercept model = sm.Logit(y, X) result = model.fit() print(np.exp(result.params)) #odds ratio

Interested in learning how we achieved same results for R vs SAS? Visit our Survival Analysis GitHub page

CAMIS-ONCO Future:

Oncology endpoint Algorithms and same Statistical results between different programming languages will provide flexibility to select different languages and eliminate risk while implementing analysis and validation. Hybrid programming languages may help draw better correlation, enhanced visualization of patient data, and strict validation of results.

Innovation can be achieved in cancer endpoint analysis, through standardization of derivations – **Algorithms** that can generate same results in Open-Source languages, later evolve as **Machine learning models (ML).**

Probably we can implement **AI tools** to efficiently achieve prespecified analysis of end-points, saving time, resources and bringing better care to patients. However, multiprogramming in analysis and validation is the first step.

Interested in FDA's perception on AI/ML in Drug Development?

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Interested in Collaboration with CAMIS-Onco group or Contributing to our White paper?

Please Get in Touch !

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