phuse

21 Jul 2022 | Springfield, PA

Agile Data Reviews

Key to smarter and leaner trials

(Lessons learnt from COVID-19 Pandemic)

Know the presenter- Nithiya Ananthakrishnan

Nithiyanandhan Ananthakrishnan
Founder & CEO, Algorics

Nithiya is a passionate life science professional with over 18 years of dedicated clinical research industry experience in the areas of clinical technologies & data science

He is currently CEO of Algorics, a fast-growing, clinical data science company focused on data management, biostatistics, data standardization, risk-based quality management and advanced data analytics

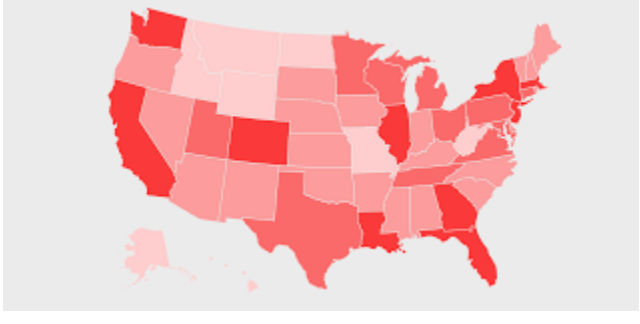
Prior to Algorics, Nithiya was associated with ICON clinical research and Cognizant technology solutions in various management roles including leading large, diverse cross-functional groups in clinical technologies and statistical programming

He is a proud recipient of PharmaVOICE 100 award in 2017 and a recognized industry thought leader associated and presenting in various industry associations and forums (SCOPE, CBI-RBM, Arena, eClinical forum, PhUSE, IASCT, DIA) in the field of clinical data value chain, SAS programming, risk-based monitoring and machine learning.

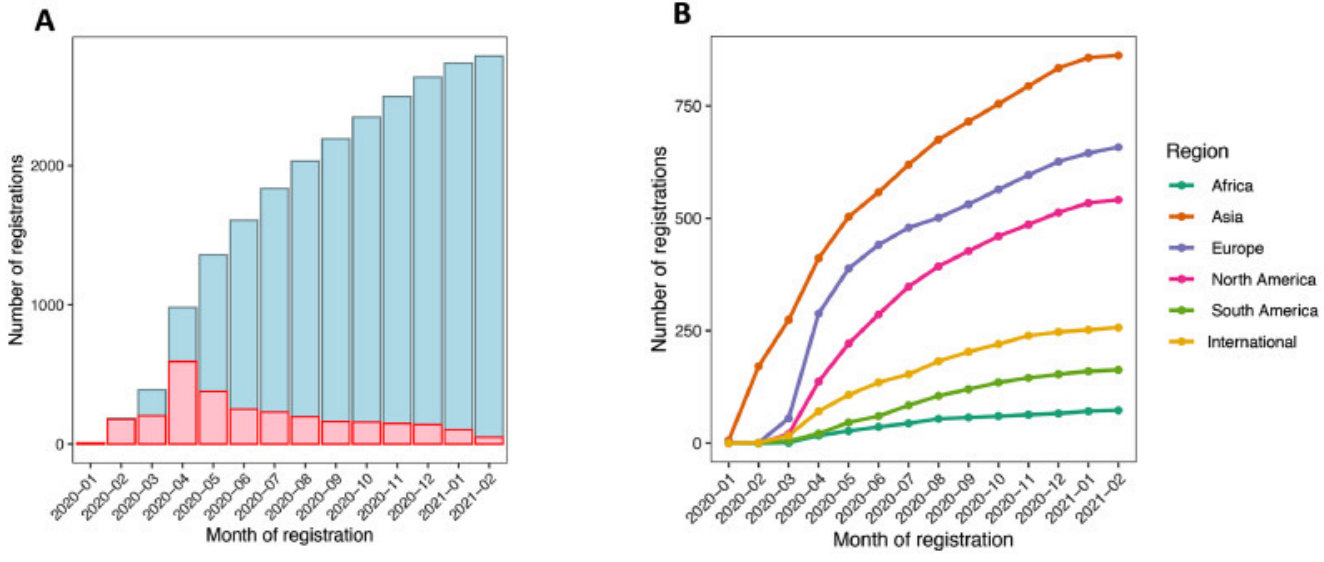
Agenda

- COVID-19 Challenges & Response
- Evolved best practices
- What are agile reviews and why do we need them?
- Implementing systems and processes for data visualization
- Key take aways

Rewind << APR 2020 << FEB 2021



RCT registrations



- Number of registrations over time. (**A**) Cumulative registration (**blue**) and number of registrations per month (**red**). (**B**) Cumulative number of registrations per month according to continent. Sixteen trials were registered before January 1, 2020 and adapted their protocol to include patients with COVID-19.

RCTs assessing vaccines and interventions

Intervention	Trials, n (%)	Planned cumulative sample size	Planned median sample size [IQR]	RECOVERY results release date	Trials registered before/after RECOVERY, n	RECOVERY results: 28-day mortality, relative risk (95% CI)
Hydroxychloroquine	304 (10.8)	436,403	160 [63-510]	June 5, 2020	243/60	1.09 (0.97-1.23); 4716 patients
Ritonavir	117 (4.2)	409,220	100 [60-326]	June 29, 2020	92/25	1.03 (0.91-1.17); 5040 patients
Lopinavir	100 (3.6)	407,846	115 [60-484]	June 29, 2020	81/19	1.03 (0.91-1.17); 5040 patients
Azithromycin	86 (3.1)	70,872	160 [60-310]	December 14, 2020	84/2	0.97 (0.87-1.07); 7763 patients
Convalescent plasma	82 (2.9)	23,844	128 [58.5-376]	January 15, 2021	79/3	1.04 (0.95-1.14); 10,406
Tocilizumab	54 (1.9)	77,805	188 [78-310]	February 11, 2021	54/0	0.86 (0.77-0.96); 4116 patients
Dexamethasone	35 (1.2)	10,033	121 [62-300]	June 16, 2020	10/25	0.83 (0.75-0.93); 6425 patients
Vaccine	175 (6.2)	899,808	900 [200-3000]			
Chloroquine	66 (2.3)	196,971	120 [60-300]			
Remdesivir	44 (1.6)	354,375	650 [152-2160]			

- on the basis of 2814 RCTs registered as of February 16, 2021 (RECOVERY)
- CI, confidence interval; IQR, interquartile range; RCT, randomized controlled trial; RECOVERY, Randomised Evaluation of COVID-19 Therapy.

Industry best data practices

1. Master protocols & CRFs
2. Estimand framework
3. Shift from “learn and confirm” to “learn as you go”
4. Lessons from Ebola outbreak
5. Multiple interim reviews, IDMC to determine safety and acceptable dose
6. Adaptive designs (allowing modifications on population and dose regimen)
7. Standardized clinical outcomes assessments
8. Standardized core data elements for evidence synthesis
9. Structured data sharing
10. Meta analysis and Network Meta-Analyses

Data review redundancy

Clinical Data

Site

- Clinical operations (CRAs)
- Medical monitors
- Project manager
- Data managers
- Biostats and programming

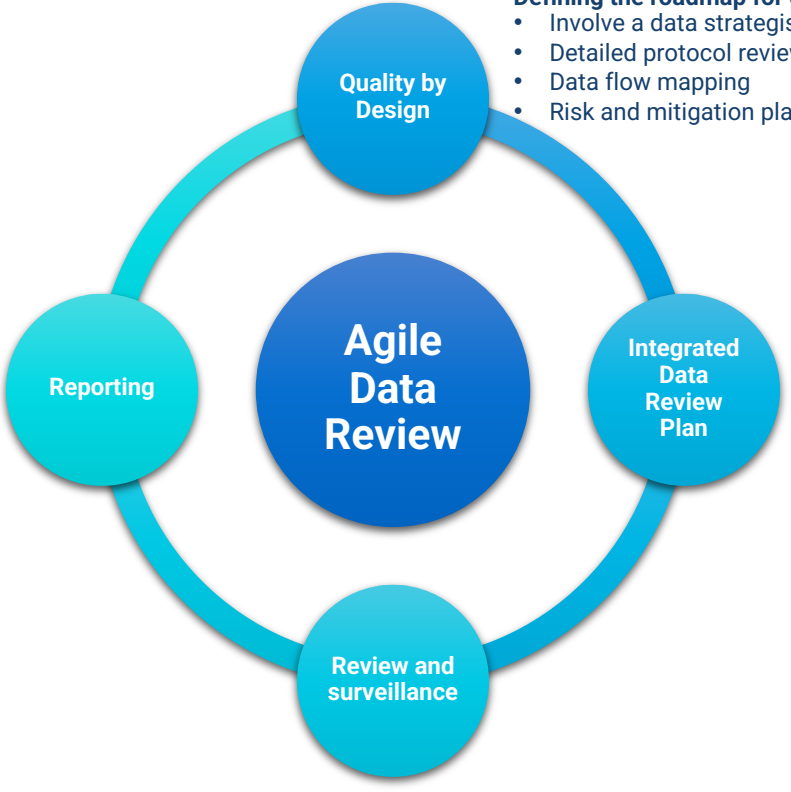
- Clinical monitoring plan
- Medical monitoring plan
- Project plan
- Data management plan
- SAP

Since data is being in silos, sites are typically responding to multiple depts separately

Review plans aren't synchronized for holistic reviews

Agile data review methodology

Defining the roadmap for data collection
- Involve a data strategist right from the start
- Detailed protocol review
- Data flow mapping
- Risk and mitigation planning



Audit and reporting ready data anytime
- Data cleaning ahead of time to reduce the time spent for interim/final data analysis

Who-What-When?
Synchronization and accountability
- Single data review workflow for effective collaboration and accountability

Data review and assessment of review compliance against key review metrics

Core data elements - Review

Data group	Data items
Overall	SDTM trial summary domain; date of randomization
Demographics	Age; gender; race; ethnicity; country; state
Medical history	Smoking use; on oxygen prior to COVID-19; recent surgery; other procedures; significant comorbidities (e.g., renal disease, cancer, cardiovascular disease, diabetes, asthma, emphysema, COPD) and immunocompromised persons (e.g., HIV infected patients, organ transplant recipients, or patients receiving cancer chemotherapy)
Medications	Concomitant medications at screening; concomitant medications during the trial
Treatment Setting	Setting (inpatient, or inpatient on mechanical ventilation); name and location (i.e., country, state) of facility
Onset History	Date symptom first reported; COVID-19 testing method; sample collection, sample collection date; COVID-19 diagnosis; diagnosis date; COVID-19 symptoms (e.g., temperature/fever, cough, sore throat, shortness of breath, etc.)
Vital signs	Weight; height; BMI; blood pressure; heart rate; pulse rate; temperature; oxygen saturation/flow rate (e.g., SpO2, FIO2); respiratory rate (breaths per minute)
Intervention/Supportive Care/Standard of Care at randomization	Medication name (including dosage, start and end date) including COVID-19-specific medications; oxygen use (in L/min) and start date (by prongs or masks); on-ventilation (noninvasive or invasive, including start date); CPAP with start date; ECMO with start date; other cytokines-administered (e.g., IFN-gamma, TNF-alpha, IL-1, GM-CSF, etc.); pressors, vasopressors or inotropes use including start date; continuous renal replacement therapies and date
Laboratory findings	COVID-19 serologies; CBC with full WBC differentials; liver function test; drug-/disease comorbidity-specific lab measures (e.g., cardiac tests, inflammation tests, diabetes tests, renal tests, IL-6)
Outcome measures (COVID-19 status and progression post-randomization)	Ordinal scale score; death from any cause (including date of death and cause of death); hospitalization (including admission and end date); intensive care unit (including admission and end date); supplemental oxygen (including type, start and end date); ventilator (noninvasive or invasive, including start and end date, or ventilator-free days); CPAP (including start and end date); high flow nasal cannula oxygen delivery (including start and end date); ECMO (including start and end date); vasopressors (including start and end date); dialysis (including start and end date); COVID-19 symptoms; NEWS2 score*; Extrapulmonary complications: stroke (NIH Stroke Scale/Score [NIHSS] ≤ ≤ 14), meningitis, encephalitis, myelitis, myocardial ischemia, myocarditis, pericarditis, pericarditis, symptomatic congestive heart failure, arterial or deep venous thrombosis
Adverse events/serious adverse events	MedDRA version; Treatment-emergent adverse events (TEAE); AE severity; serious AE

Key questions before building visualization

What data do we need?
Identify critical data points and processes

How does the data come into our systems?
What infrastructure do we need to bring this data in?.

Who are the end users?
Multiple departments/ functions that will be reviewing the data

How frequently do dashboards update?
Set expectations for what is real-time?

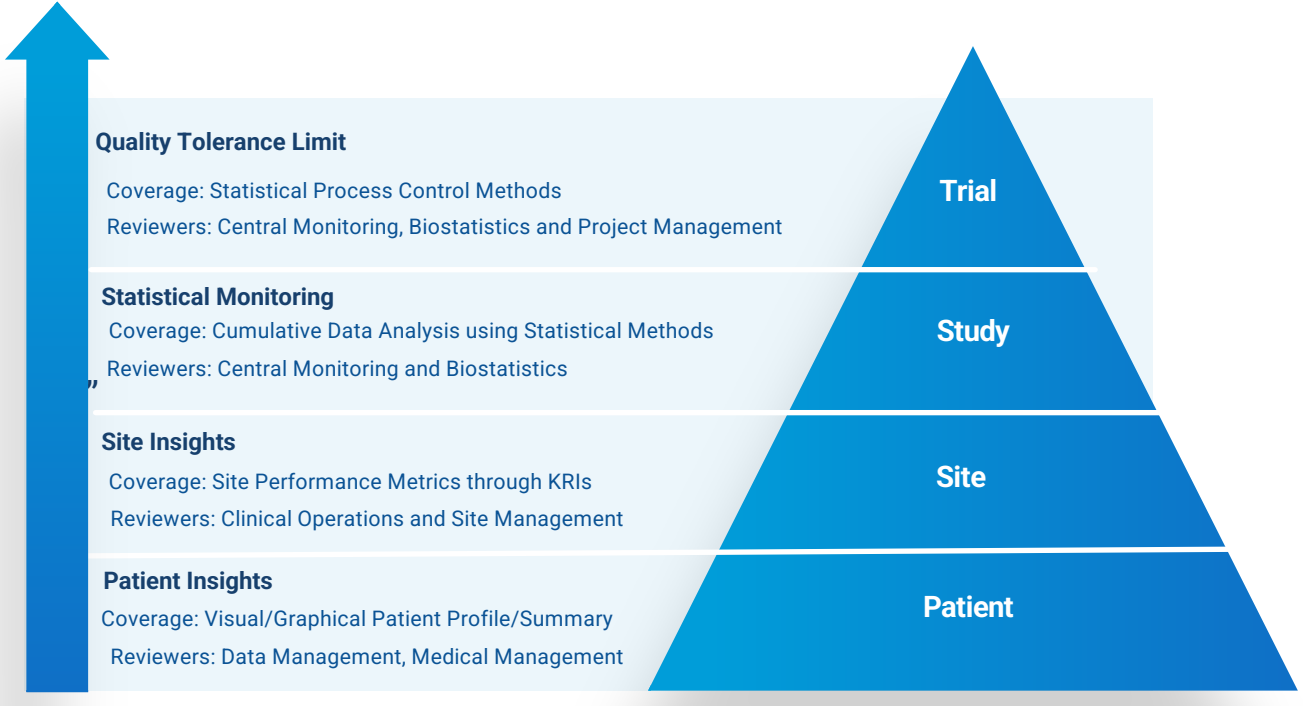
What is the ideal reporting format?
The visualizations that work best for our data points

To what level of data drilling can we facilitate?
How much detail can this dashboard provide and is that aligned?

Implementing a visual data review system

5 steps to building a visual output

Rolling up multi-level data visualization



4 hierarchical levels of review

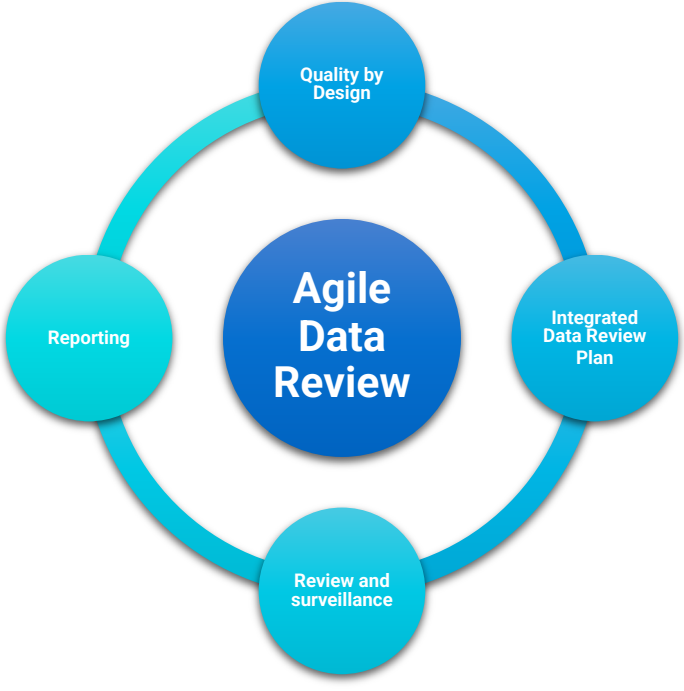
- Trial level
- Study level
- Site level
- Patient level

- Inventory-based standard risks and visualizations
- Critical data-based custom risks and visualizations
- Patient-level visualization for near real-time subject data review
- Study level statistical monitoring visualizations for fraud detection (minimum 20 sites and minimum 4- 5 subjects per site)

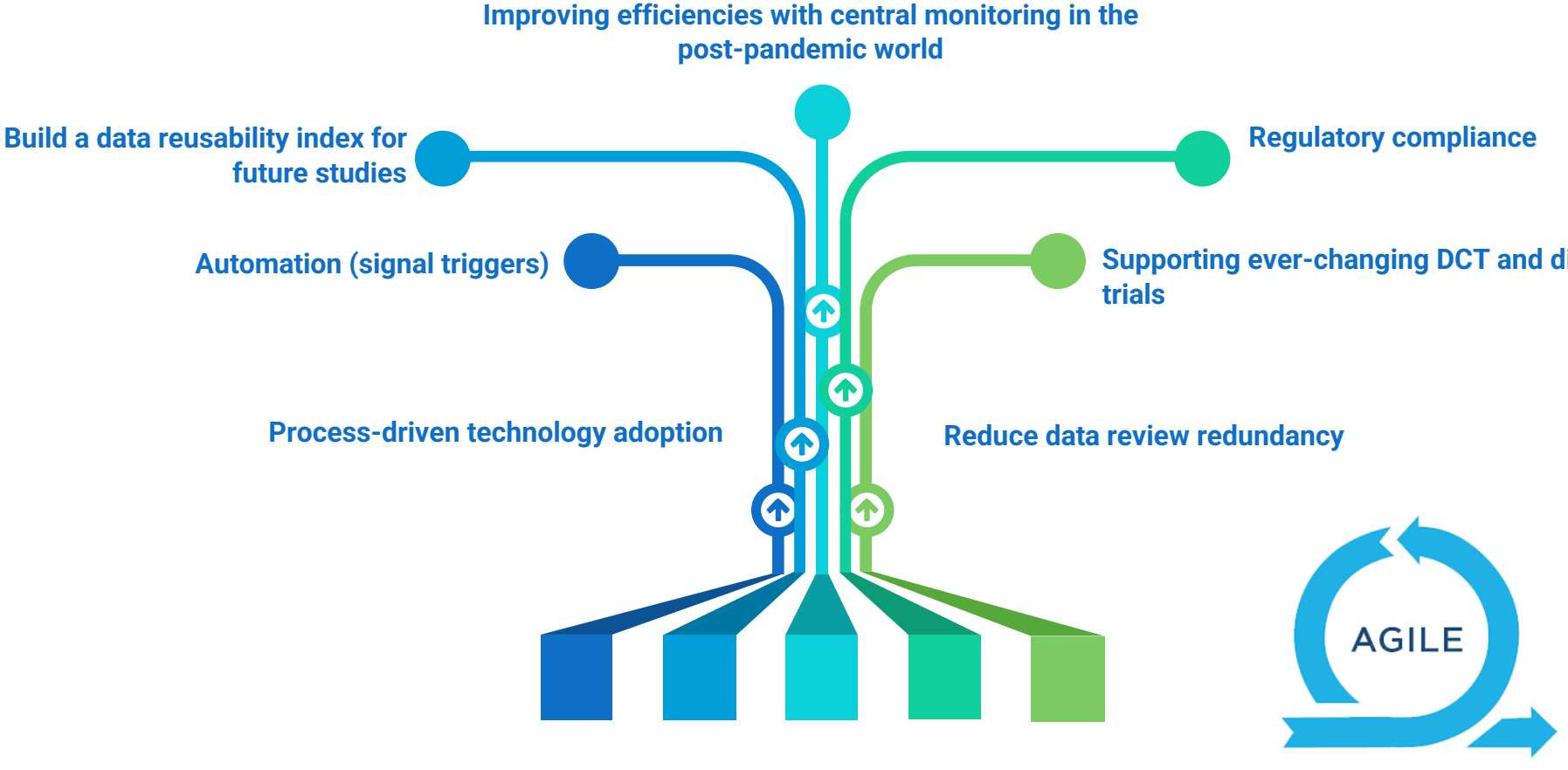
Agile review process

Steps:

- **Acquire:** Collect focused and critical data at one place
  - Demographics
  - Disease condition
  - Intervention vs Standard of care
  - Dosage
  - Targeted outcome
- **Prepare:** Data transformation for analysis making it scalable and re-usable
  - Setup of automated data transformation – Standard data review model
- **Analyze/Review:** Data output review by SMEs
  - Consistent visualization that can be interpreted across trials/ teams
- **Act:** Translate data into actions
  - Pre-set rules and mitigations based on tolerance limits for go-no-go decisions



Difference made by an agile data review ecosystem



References

•Akacha, M., Branson, J., Bretz, F., Dharan, B., Gallo, P., Gathmann, I., Hemmings, R., Jones, J., Xi, D., and Zuber, E. (2020), "Challenges in Assessing the Impact of the COVID-19 Pandemic on the Integrity and Interpretability of Clinical Trials," *Statistics in Biopharmaceutical Research*, 12, 419–426. DOI: https://doi.org/10.1080/19466315.2020.1788984. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Best, N, Perevozskaya, I., Lunn, D., Archer, G., Euesden, J., Fillmore, C., Sherina, V., Thompson, D., and Zwierzyna, M. (2021), "Predicting the COVID-19 Pandemic Impact on Clinical Trial Recruitment," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2021.2000487. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Chakladar, S., Liao, R., Landau, W., Gamalo, M. and Wang, Y. (2021), "Discrete Time Multistate Model With Regime Switching for Modeling COVID-19 Disease Progression and Clinical Outcomes," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2021.1880966. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Hamasaki, T., Bretz, F., Cooner, F., LaVange, L.M., and Posch, M. (2020), "Statistical Challenges in the Conduct and Management of Ongoing Clinical Trials During the COVID-19 Pandemic," *Statistics in Biopharmaceutical Research*, 12, 397–398. DOI: https://doi.org/10.1080/19466315.2020.1828692. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•McMillan, G., Mayer, C., Tang, R., Liu, Y., LaVange, L., Antonijevic, Z., and Beckman, R.A. (2021), "Planning for the Next Pandemic: Ethics and Innovation Today for Improved Clinical Trials Tomorrow," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2021.1918236. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Meyer, R.D., Ratitch, B., Wolbers, M., Marchenko, O., Quan, H., Li, D., Fletcher, C., Li, X., Wright, D., Shentu, Y., Englert, S., Shen, W., Dey, J., Liu, T., Zhou, M., Bohidar, N., Zhao, P.L., and Hale, M. (2020), "Statistical Issues and Recommendations for Clinical Trials Conducted During the COVID-19 Pandemic," *Statistics in Biopharmaceutical Research*, 12, 399–411. DOI: https://doi.org/10.1080/19466315.2020.1779122. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Mukherjee, R., Yajnik, P., Muhlemann, N., and Morgan-Bouniol, C. (2021), "A Sequential Predictive Power Design for a COVID Vaccine Trial," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2021.1979641. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Natanegara, F., Zariffa, N., Buenconsejo, J., Liao, R., Cooner, F., Lakshminarayanan, D., Ghosh, S, Schindler, J.S., and Gamalo, M. (2021), "Statistical Opportunities to Accelerate Development for COVID-19 Therapeutics," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2020.1865195. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

•Patterson, S., Fu, B., Meng, Y., Bailleux, F., and Chen, J. (2021), "Statistical Observations on Vaccine Clinical Development for Pandemic Diseases," *Statistics in Biopharmaceutical Research*, DOI: https://doi.org/10.1080/19466315.2021.1919197. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

THANK YOU

Contact:
Nithiya Ananthakrishnan
(Nithiya@algorics.com)

The Global Healthcare Data Science Community

Contact Channels
UK +44 1843 609600
office@phuse.global
phuse.global

Social Media
@phusetwitta
/phusebook
/phusetube
/company/phuse