

COVID-19 and Clinical Trials: The Medidata Perspective

Release 4.0

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What's New/What's Significantly Updated in Release 4.0

- New: Results of a global survey of investigator sites about the impact of COVID-19 on their clinical trials
- Updated: Metrics on new patients entering trials by country and therapeutic area (full month data for March and April)
- Updated: Metrics of impact of COVID-19 on number of site visits.
- New: Summary table of the current 8 vaccine clinical trials for COVID 19
- New: Launched the COVID-19 Symptom Tracker as part of Medidata's Patient Portal, myMedidata
- New: The updated MedDRA 23.0 dictionary supporting new COVID-19 terms and revisions is now available to clients using Rave Coder.

COVID-19 Impact on Clinical Trials:

NEW SITE SURVEY REVEALS

The COVID-19 pandemic has turned the world upside down; it's hard to think of an activity, business, or goal that hasn't been impacted. Clinical trial sites are no exception.

Globally, thousands of these sites are collectively the largest group of users of Medidata technology and solutions, which support the most efficient, safe, and accurate drug development process possible. To better understand how the pandemic is impacting their vital work and to gain insight into how they are adjusting to this new reality, we fielded a global online survey. Their responses paint a revealing picture of their concerns and flexibility.

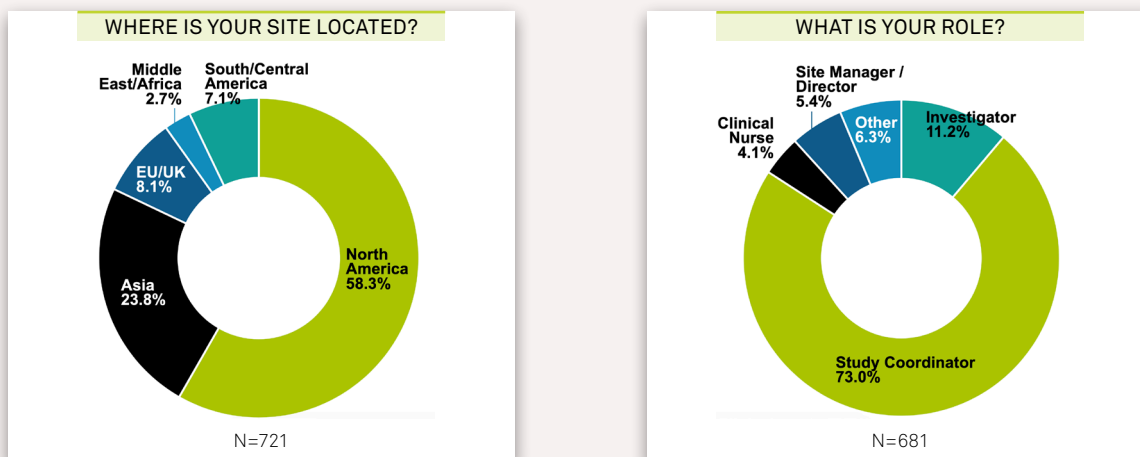
ABOUT THE SURVEY

On April 23, 2020, Medidata successfully delivered 9,952 electronic surveys to personnel at investigator sites using our technology that supports their clinical trials. On April 27th, we sent an email reminder to 6,599 non-respondents. The survey was closed at 5pm EDT on April 29, 2020. The results are summarized below.

RESPONSE RATE BY WHOM AND FROM WHERE

There were 1,030 respondents who answered at least one question of the survey for a **response rate of 10.4 percent**. Of those who answered the questions, 58.3 percent were from the United States (North America) and 23.8 percent were from Asia. Of those who answered the question, 73.8 percent identified their role as Study Coordinator and 11 percent were Investigators. (See Figure 1).

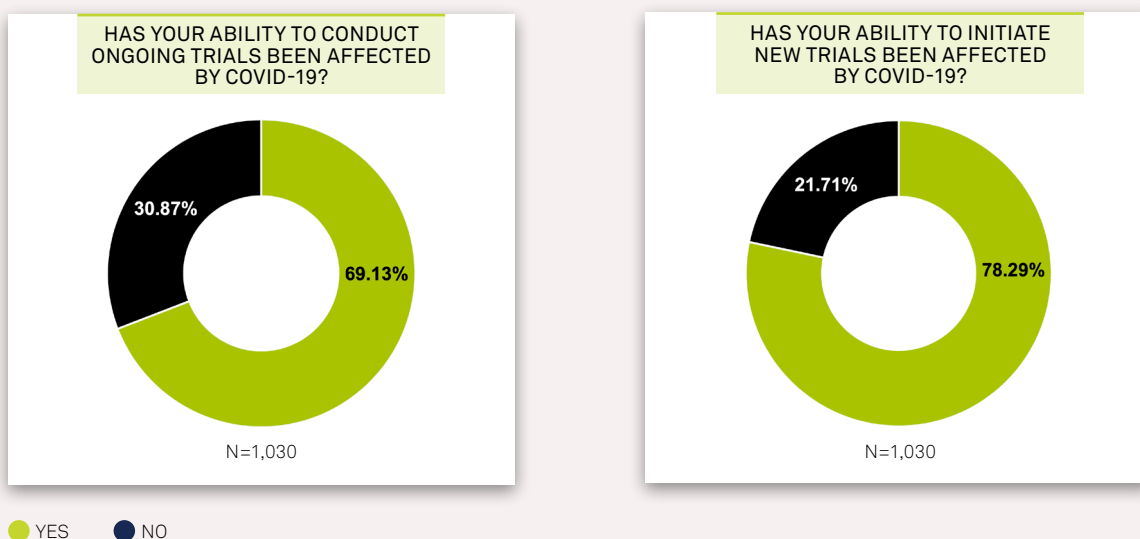
Figure 1. Site Location/Respondent Role



THE PANDEMIC IS A SIGNIFICANT FACTOR IN STUDY CONDUCT

The pandemic and various “lockdown” measures put in place around the world are impinging on sites’ ability to both conduct existing trials and to initiate new trials. For **69 percent** of respondents, COVID-19 has affected their ability to conduct **ongoing** trials, while **78 percent** of respondents believe that COVID-19 has impacted their ability to **initiate new** trials. (See Figure 2).

Figure 2: Impact of COVID-19 on Ongoing Trails and Ability to Launch New Ones

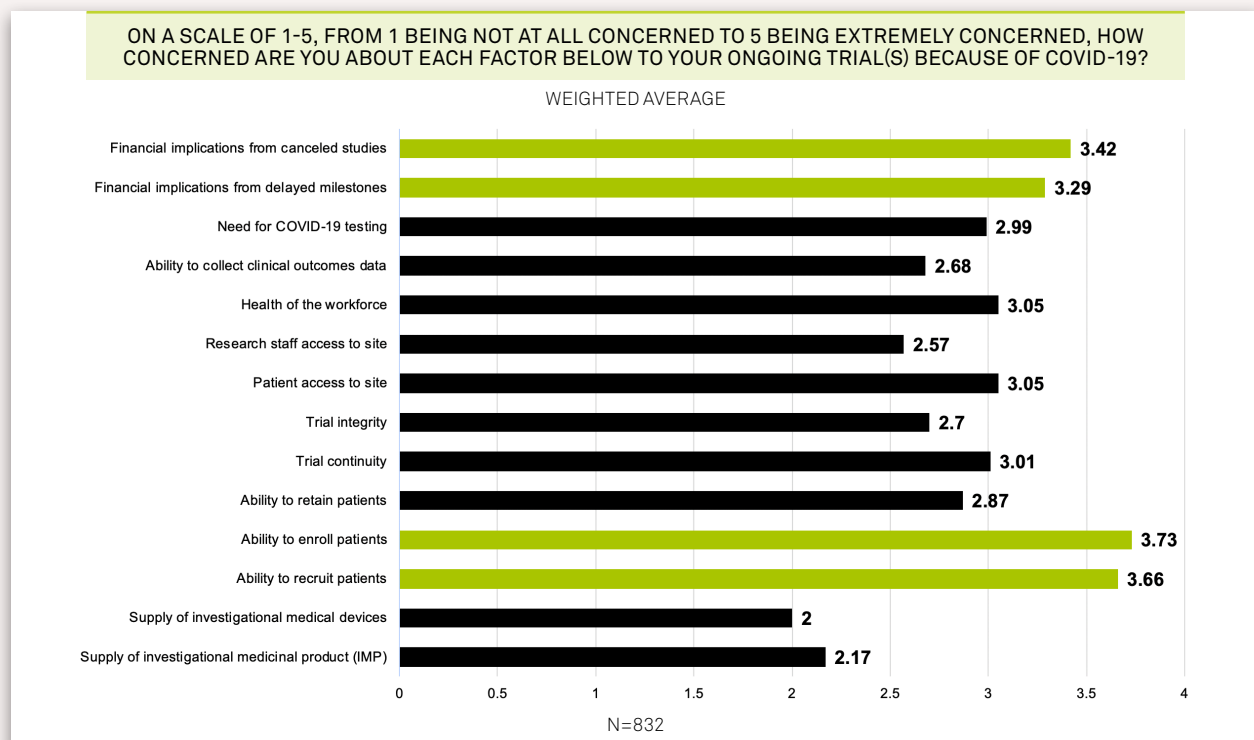


SITES ARE MOST CONCERNED ABOUT PATIENT RECRUITMENT/ENROLLMENT

Respondents were asked to rate their level of concern on a variety of factors ranging from the supply of investigational products... to their ability to recruit and enroll patients... to the health of the workforce and their ability to collect outcomes data. The scale was from one to five, with one being not at all concerned and five being extremely concerned.

The top four concerns expressed by the respondents based on the weighted average of the answers were: **ability to enroll patients** (3.73); **ability to recruit patients** (3.66); **financial implications for canceled studies** (3.42); and **financial implication from delayed milestones** (3.29). Other noteworthy concerns were: **patient access to the site** (3.05); **health of the workforce** (3.05) and **the need for COVID-19 testing** (2.99). (See Figure 3). By far, respondents expressed the greatest concern over patient recruitment and enrollment; well over half rated their concern as a four or five for both of these topics. (See Figure 3).

Figure 3: Level of Concern of COVID-19 Impact on Trial-Related Activities



In looking behind the weighted average, we see that responses on trial continuity, trial integrity, the health of the workforce, and the need for COVID-19 testing were distributed widely across the spectrum from “not at all concerned” to “extremely concerned.” Respondents indicated strong confidence in the **ongoing supply of investigational medicinal products (IMP)** as well as **investigational medical devices**. The percentages that described themselves as “extremely concerned” were **seven percent for IMP** and only **four percent for medical devices**.

Few were concerned about their **ability to collect clinical outcomes data**; only **11 percent** reported being “**extremely concerned**,” while almost half (49 percent) described themselves as “not at all concerned” or only “somewhat concerned.”

SITES ARE MITIGATING ISSUES IN A NUMBER OF WAYS

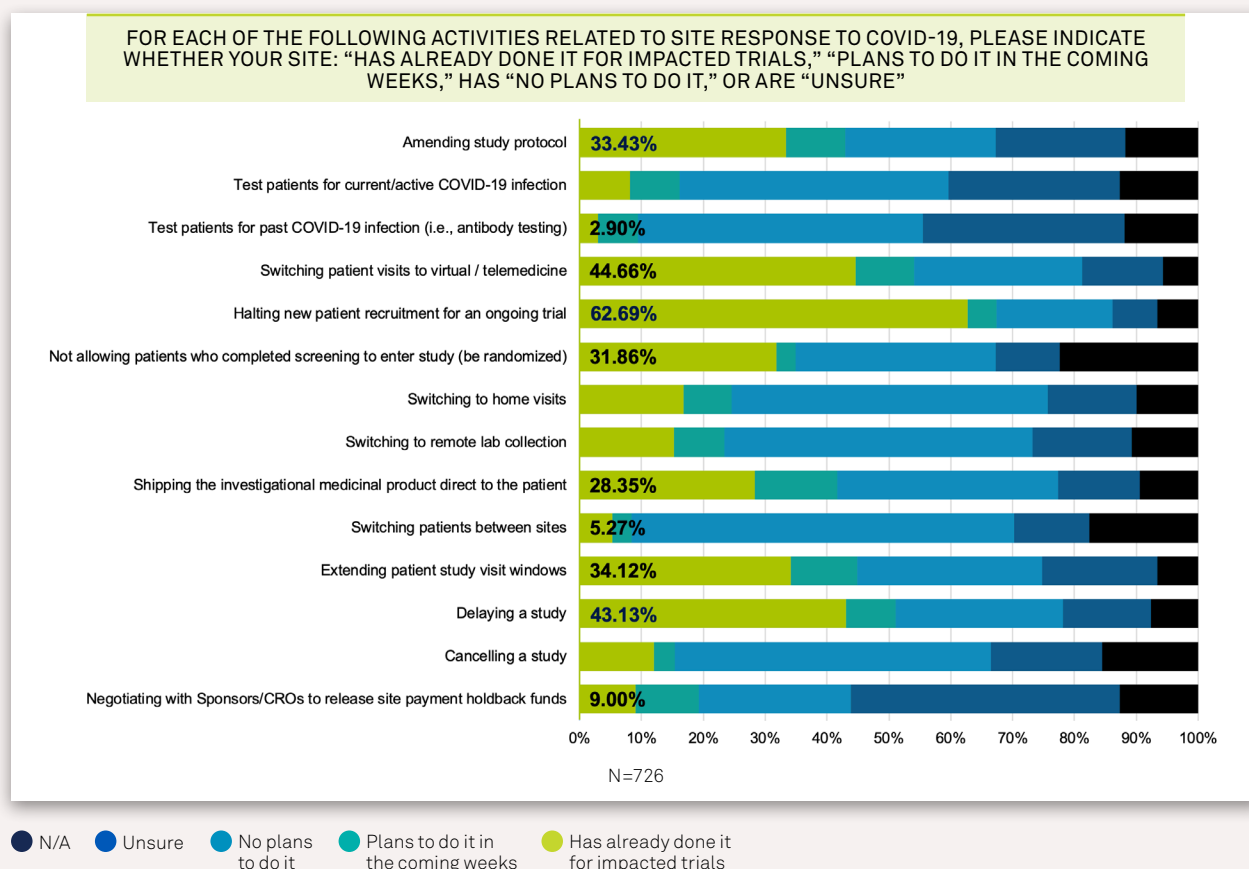
Given the health implications of the novel coronavirus and the practical considerations of managing patient contacts, sites have taken a variety of measures to limit patient exposure. Respondents were asked to indicate for a number of activities whether their site “Has already done it for impacted trials,” “Plans to do it in the coming weeks,” has “No plans to do it,” or are “Unsure.”

The top five activities already undertaken by sites in response to COVID-19 are: **halting new patient recruitment for an ongoing trial (63 percent)**, **switching patients to virtual/telemedicine (45 percent)**, **delaying a study (43 percent)**, **extending patient study visit windows (34 percent)** and **amending study protocols (33 percent)**. (See Figure 4). Roughly a third (32 percent) have **not allowed patients who have completed screening to be randomized**.

Switching patients between sites has rarely been used as a solution, with only **five percent** having done so. And, the percentage of sites that has cancelled **studies (12 percent)** is relatively small.

Somewhat surprisingly, relatively small numbers have tested patients for current/active or past COVID-19 infection. Only **eight percent** have **tested patients for active infection** and only **three percent** have **tested patients for prior infection**. (See Figure 4).

Figure 4: Activities Done/Planned based on COVID-19



SUGGESTIONS FROM THE FRONTLINE

When asked to name the “one thing that could help you meet your clinical trial milestones that is currently not in place,” respondents offered voluminous suggestions for Sponsor policies and support from Contract Research Organizations (CROs). Respondents appeared eager to share their ideas, which included:

- **Examine the global impact of decisions**
 Although COVID-19 is widespread, all parts of the world aren’t impacted equally. Decisions to postpone a new study or to halt recruitment that apply universally around the globe, unnecessarily impact research in those areas where it is safe to continue screening and enrolling patients.
- **Provide greater flexibility and understanding**
 Many sites wanted Sponsors and CROs to appreciate the fact that work cannot proceed under the rules of business as usual. Things must be done differently, or according to different timelines. For example, it may take longer to resolve data queries as staff may not be on site most of the time. And, to accommodate patients, study visit windows may need to be extended.
- **Adopt telemedicine**
 Sites suggested a number of solutions to accommodate patients who can’t visit research centers. These included: using online questionnaires for patients, e-consent, amending protocols to include virtual visits and home-care nursing, sending investigational products directly to patients, reviewing and revising endpoints that require long-term, direct contact with patients, and adopting secure means for patients to communicate and share information with sites from home.
- **Provide additional financial support**
 Sites mentioned that when studies are suspended or when milestones are extended, their revenue is negatively affected, although they must continue to employ study coordinators. Suggestions ranged from making contract amendments for increased remote monitoring work to increasing overhead reimbursements.
- **Develop contingency plans**
 In light of how sites have had to respond to the emergency created by the pandemic, it was suggested that Sponsors and CROs develop study-specific contingency plans that can automatically be activated in the event of another outbreak. The plan should include provisions for transporting patients, for switching from a central lab to local labs, and for the proactive supply of PPEs, to name a few. This would prevent deviations from scheduled visit windows and outline systemic solutions without compromising patient safety.

RESEARCH, INTERRUPTED

Sites are on the frontline of experiencing the impact of COVID-19, and the pandemic has directly and dramatically impacted their ability to continue their work, which ultimately will impede development progress.

Not unexpectedly, most sites are feeling the negative impact of the pandemic on current and future trials, specifically around delays in patient enrollment and recruitment. They also are concerned about the impact of trial delays and cancellations on their financial well-being. Over two-thirds of respondents indicated that they have halted, or will soon halt, patient recruitment for ongoing trials, a third are halting randomization, and about half are now delaying or will be delaying their studies.

Sites have shown flexibility and ingenuity in adopting new approaches. Over half of sites are switching site patient visits to virtual ones and/or are using telemedicine to interact with patients - most likely through protocol amendments.

The results are consistent with other data previously presented by Medidata and indicate the growing risks associated with new study starts, trial progression and completion as well as impact on the sites themselves from a financial and work safety perspective.

Insights to Ongoing Data Capture in Clinical Trials

Medidata is continuously monitoring COVID-19's global impact on clinical trials. Our first data and insights impact report was released on March 23 with subsequent releases on April 3, April 17 and May 4. Medidata's analysis of the decline in new patients entering clinical trials for actively recruiting studies demonstrates the growing significance of the pandemic's impact on cities, regions, and countries with increasingly tighter laws and guidelines restricting movement by anyone outside of the home.¹

Updates to the April 3 and April 17 analyses were performed on May 1, 2020 and the results for the month of April are shown next to March (See Figure 5). Currently, the global data shows a 79% decrease in the average number of new patients entering trials per study-site YoY during the month of April compared to the same time frame last year.¹ During March there was a 65% decrease. The data clearly indicates that the impact of the pandemic on new patient enrollment in most countries continues to grow. Only China, South Korea and to a lesser extent Italy, saw a decrease in impact.

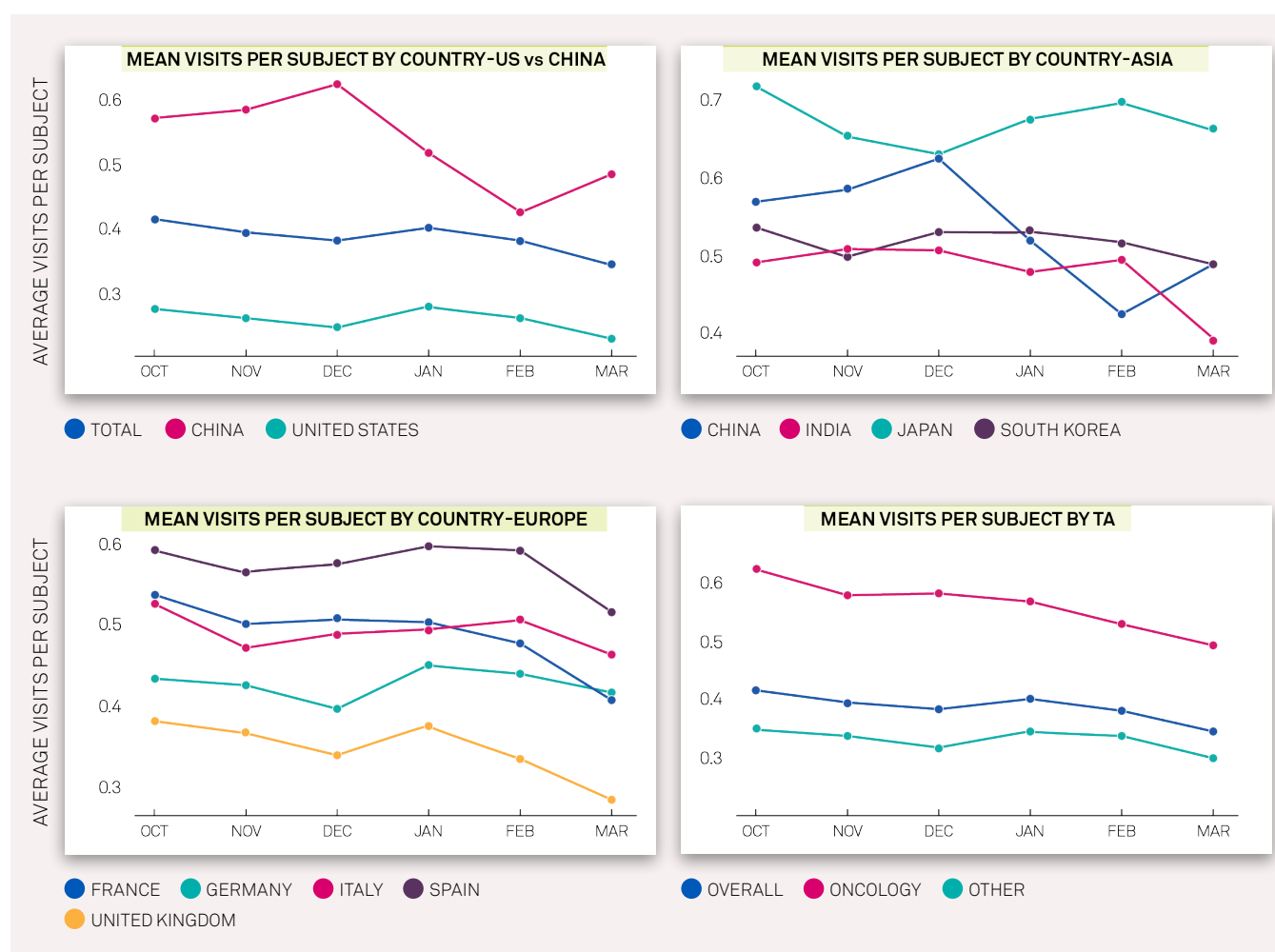
Figure 5: Impact of COVID-19 on New Patients Entering Trials

| | | YoY Difference (%) Mar 2020 vs. Mar 2019 | YoY Difference (%) Apr 2020 vs. Apr 2019 |
|-------------------------------|--------------------|---|---|
| All Countries, All TAs | All | -65.5% | -79% |
| Asia | China | -68% | -33% |
| | India | -84% | -97% |
| | Japan | -44% | -69% |
| | South Korea | -61% | -42% |
| Europe | France | -68% | -81% |
| | Germany | -33% | -77% |
| | Italy | -53% | -49% |
| | Spain | -68% | -82% |
| | United Kingdom | -80% | -95% |
| North America | United States | -66% | -83% |
| Therapeutic Area | Cardiovascular | -69% | -95% |
| | CNS | -68% | -76% |
| | Dermatology | -64% | -91% |
| | Endocrine | -81% | -88% |
| | ID/Anti-Infectives | -47% | -66% |
| | Oncology | -48% | -60% |
| | Respiratory | -34% | -86% |

¹ Analysis across 4,667 studies and 185,949 study-sites

Additionally, we are adding an update to the visit-per-study-subject analysis in on-going studies (See Figure 6). As we shared in our last release, both globally and in the US specifically, there has been a 17% decrease in visits per subject between Oct 2019 and March 2020. In Asian countries, the picture is mixed. As indicated in the last release, China saw a recovery in visit per subject between February and March 2020, after seeing a steep decline between October and February. India is seeing an impact similar to the one on the global scale, with a decrease of 20% between October 2019 and March 2020. South Korea and Japan saw a lesser impact. In Europe, the strongest declines occurred in France and the UK, with a 24% and 25% decrease between October 2019 and March 2020, respectively. From a TA perspective, the impact on visit-per-study-subject was higher in Oncology, with a 21% decrease from October 2019 to March 2020. We will continue to update and refine this metric in upcoming releases.

Figure 6: Impact of COVID-19 on Site Visits



Understanding what is happening on the ground is critical to define a path forward. We will continue to publish updated analyses on overall industry trends throughout this pandemic and beyond.

Regulatory Response

As of April 30, many authorities including the [European Medicines Agency \(EMA\)](#), [U.S. Food and Drug Administration \(FDA\)](#), [UK Medicines and Healthcare Products Regulatory Agency \(MHRA\)](#), Germany ([BfArM](#)), France ([ansm](#)), Netherlands ([ccmo](#)), Ireland ([HPRA](#)), Denmark ([Sundhedsstyrelsen](#)), Switzerland ([swissmedic](#)), Japan ([PMDA](#)), South Korea ([MFDS](#)), [Health Canada](#), Australia ([DoH](#)), and Singapore ([HSA](#)), have provided updated emergency guidance on trial conduct during the pandemic. In addition, multiple stakeholder organizations including the [Association of Clinical Research Organizations \(ACRO\)](#) and multiple IRBs (an example [here](#)) have issued guidance documents as well. What's clear is that regulations and guidance differ from country-to-country.

Due to the recent disruptions and challenges posed by COVID-19, activity promoting the use of technology in clinical trials has increased. Additionally, regulators and stakeholder groups are demonstrating pragmatism and flexibility in terms of mitigating when possible. Common topics include: triggers for protocol amendments and deviation processes, risk assessment expectations, continuing or halting a trial, continued subject participation, informed consent - including eConsent (FDA), and remote monitoring (see 16 April FAQ update). Note that while the US FDA, UK MHRA, Australia DoH, Health Canada, and Singapore HSA suggest remote source data verification is possible, the EMA leaves it as an option in very limited circumstances ([Section 11 and Annex](#)). Centralized monitoring activities are suggested by most regulators however.

For more detailed information on the global regulatory responses to the impact of COVID-19 on clinical studies, visit Medidata's blog [here](#).

Impact to Medidata Customers, Patients and Trials

Real-time and detailed reporting and analytics are critical for sponsors and CROs to assess the day-to-day impact of the pandemic on a trial at the patient, site and country level and so they can quickly implement changes to mitigate the risk of trial failure.

Rapid and safe implementation of protocol amendments is vital to address both site closures and the fact that trial participants no longer receive or have access to the investigational product. Inaccessible sites mean that alternative, remote approaches to drug supply, monitoring study conduct, compliance, patient safety and data quality are needed. The more trials can be safely "virtualized," the more likely they will be able to successfully proceed.

As of April 3rd, several large pharma (Pfizer, Bristol Myers Squibb and Eli Lilly)² and smaller Biotech companies (Moderna Therapeutics³, Iveric Bio⁴, Aslan⁵, Provention Bio⁶ and Addex⁷) have publicly announced that they are modifying their R&D plans. Typical modifications in certain trials are some form of temporary delay in site activation and/or patient enrollment. The impact of COVID-19 on trial success is already an issue, as evidenced by Aveo Pharmaceuticals Inc. citing COVID-19 as a reason for the study failure of ficlatuzumab in acute myeloid leukemia.⁸ These growing examples of trial delays or stoppage by biopharma to mitigate the cost and impact of the pandemic dramatically highlight the need for rapid, innovative solutions to help trials successfully start, continue and finish.

The future of global public health is dependent on the scientific and medical communities' ability to find a highly effective vaccine to prevent further spread of the virus as well as mitigate the likelihood that it will reappear. As of April 30, 2020, according to the World Health Organization, there are 94 vaccine candidates in preclinical development and 8 candidate vaccines for COVID-19 in clinical evaluation.⁹ An abridged summary of these vaccines in clinical evaluation is outlined in Figure 7 below.

Figure 7: The 8 COVID-19 Vaccines in Clinical Development

| Type of Candidate Vaccine | Developer | Current Stage of Clinical Development and Regulatory Status |
|--|--|---|
| Adenovirus Type 5 Vector | CanSino Biological Inc./Beijing Institute of Biotechnology | Phase 2 ChiCTR2000031781 Phase 1 ChiCTR2000030906 |
| ChAdOx1 | University of Oxford | Phase 1/2 NCT04324606 |
| DNA plasmid vaccine with electroporation | Inovio Pharmaceuticals | Phase 1 NCT04336410 |
| Inactivated | Wuhan Institute of Biological Products/ Sinopharm | Phase 1 ChiCTR2000031809 |
| Inactivated | Beijing Institute of Biological Products/ Sinopharm | Phase 1 (regulatory approval) |
| Inactivated + alum | Sinovac | Phase 1 NCT04352608 |
| mRNA | BioNTech/Fosun Pharma/ Pfizer | Phase 1/2 2020-001038-36 |
| LNP- encapsulated mRNA | Moderna/NIAID | Phase 1 NCT04283461 |

² <https://www.fiercebiotech.com/biotech/covid-19-prompts-pfizer-to-stop-enrollment-most-studies>. Accessed April 4, 2020

³ <https://www.fiercebiotech.com/biotech/covid-19-causes-moderna-to-pause-a-clutch-clinical-trials>. Accessed April 4, 2020.

⁴ <https://www.fiercebiotech.com/biotech/iveric-bio-latest-to-be-hit-by-covid-19-as-it-delays-a-key-trial>. Accessed April 19, 2020

⁵ <https://www.fiercebiotech.com/biotech/covid-19-outbreak-prompts-provention-to-pause-diabetes-trial>. Accessed April 19, 2020

⁶ <https://www.fiercebiotech.com/biotech/covid-19-outbreak-prompts-provention-to-pause-diabetes-trial>. Accessed April 19, 2020

⁷ <https://www.fiercebiotech.com/biotech/swiss-bio-addex-halts-parkinson-s-test-as-trial-delays-tick-up-covid-19-disruption>. Accessed April 19, 2020

⁸ <https://www.reuters.com/article/brief-aveo-oncology-and-biodesix-to-disc/brief-aveo-oncology-and-biodesix-to-discontinue-cyfi-2-study-of-ficlatuzumab-idUSFWN2BK1LR>. Accessed April 4, 2020

⁹ <https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines>. Accessed May 2, 2020.

Medidata Solutions to Assist Sponsors/Partners, Patients and Trials

Medidata has solutions that can be immediately leveraged by our customers to both better understand the impact of the pandemic on their trials, and to mitigate the challenges of patients unable to visit sites for their drugs and protocol-directed clinical and patient-reported data capture.

There are **four** main categories of challenges facing clinical trials. The following is a high level summary of these challenges and the solutions that Medidata is prepared and ready to provide:

CHALLENGE 1: UNDERSTANDING THE EVOLVING SITUATION

Solutions:

- Study/sponsor level metrics and dashboards to understand impact on enrollment, patient visits, data collection, query response rates, and additional metrics to help diagnose risk areas
- Industry-wide dashboards and analysis to understand trends globally and areas of greater or lesser disruption

CHALLENGE 2: RECONSIDERING TRIAL DESIGN TO ENABLE DATA CAPTURE

Solutions:

- Shift to more virtualization – reduce patient visits; minimize site burden
- Shift site mix to lower-impacted countries / regions
- Consider Synthetic Controls to reduce patient enrollment needs

CHALLENGE 3: MAINTAINING QUALITY AND SUPPLY

Solutions:

- Centralize data oversight and monitoring activities, bringing identification of patient anomalies earlier in the process and away from onsite identification
- Closely monitor patient volume and drug supply to minimize supply disruptions

CHALLENGE 4: ACCELERATING STUDY START UP

Solutions:

- Sponsors focused on developing vaccines against, and treatments for COVID, must safely and effectively accelerate study start up times through faster investigator budgeting, so cures and treatments can get to market faster

Details on New and Adapted Medidata Solutions

The following tables provide details about the Medidata's solutions available now to assist with your trial challenges. Since some aspects of the four challenges are not mutually exclusive, some solutions may be applicable to more than one challenge.

CHALLENGE 1: UNDERSTANDING THE EVOLVING SITUATION

Acorn AI Intelligent Trials

CHALLENGE

Understanding the country/site/disease area impact across the industry, and developing risk mitigation and recovery plans

***New Medidata Solution**

SOLUTION

COVID-19 Trial Impact Analytics*: Data and analytics to develop industry tracking, forecasting and deep dives for priority studies to support client's COVID-19 impact assessment, risk mitigation and recovery decisions.

Situation Tracking

- Deploy standard reports to track impact of COVID-19 for Client and industry
- Data tracked - measures of enrollment and data collection
- Views at study, portfolio, geography level

Impact Forecasting

- Overlay trends in COVID-19 testing and infection rates with impact on trials to understand leading indicators of slowdown
- Identify markers of recovery at a country and region level

Recovery Planning

- Recovery planning / scenarios for acceleration across portfolio
- Deep dive in priority studies

CHALLENGE 2: RECONSIDERING TRIAL DESIGN TO ENABLE DATA CAPTURE

Rave eCOA

CHALLENGE

Provide ways for missed or risked visit forms to be remotely filled out by patients on existing studies.

SOLUTION

Medidata's eCOA solution can be used to convert site-based data forms to remote data forms. If study modifications are made to accommodate this approach, patients can download the patient cloud app from the app store and provide urgent data forms as needed for missed visits. Any Rave EDC study using eCOA can have additional data forms pulled into the eCOA app and made available to patients. Any Rave EDC studies not using eCOA can add eCOA to the project and immediately begin converting forms to remote-enabled forms.

Rave eConsent

CHALLENGE

Providing remote eConsent on trials that are underway or are starting up.

SOLUTION

Currently, our iPad based consent is not set up for BYOD with a patient device. However, remote consent is possible through the use of the legacy Engage (Rave Virtual Trials/Patient Portal) platform and can be supported as a standalone activity. Some integration with Rave EDC is possible, although different usernames and passwords are used for the legacy Engage platform. The primary use case for this technology would be ongoing studies where a remote consent is required to keep the study up and running. In this case, a special instance of the Engage technology could be launched allowing patients to remotely log in and provide consent.

Rave Patient Portal / Rave Virtual Trials

CHALLENGE

Prepare for COVID-19 studies with self-quarantined patients globally.*

***New Medidata Solution**

Provide rescue and/or new study designs that enable virtualization of visits and data capture.

SOLUTION

In late April Medidata and 3DS launched a COVID-19 Symptom Tracker as part of myMedidata (Medidata's Patient Portal), which can be used as a remote patient symptom tracker. This Tracker will function as a registry (in an MVP version) and will allow sites to remotely monitor and report symptoms of patients in their trials. Learn more about myMedidata and the COVID-19 Symptom Tracker [here](#).

In ongoing studies and/or new study designs, the Rave Patient Portal can be used to virtualize more aspects of the study design. New generation versions of the portal will be released later this year but our existing technology is used today on ongoing virtual trials managing thousands of patients and is a fully functional and validated system for clinical research. In many cases, this version can be modified for a study that needs to accommodate remote consent, remote randomization, remote data capture, reporting and site access. Because this app is web-based, it is also easily available for all patients on all types of platforms and does not require a mobile device or device distribution..

Acorn AI Synthetic Control Database / Trial Design

CHALLENGE

Improving understanding of safety in experimental treatments (e.g., chloroquine) that are now under review for cross-indication use.

SOLUTION

Support research by providing aggregated data, e.g., Synthetic Control Database (SCD) to support understanding of expected and unexpected AEs for products being studied for COVID-19. These drugs are already marketed with a mature safety profile, but an SCD might improve the analyses above what published literature can provide. In addition, historical trial data can be compared against real-world data from claims or EMRs to provide confidence and validation in trial design, better understand inclusivity of patients populations to better reflect real world clinical practice, and potentially decrease sample size requirements for event-driven trials.

Closing out on-going studies given barriers completing visits.

Leveraging historical clinical trial data to augment or replace control arms of trials that are in danger of high dropout or unfulfilled enrollment due to COVID-19; reduce scientific uncertainty to advance to the next phase, reduce patient enrollment burden or increase statistical power.

Rave Coder

CHALLENGE

The coronavirus pandemic has prompted an urgent need for a harmonized, standardized approach to coding and reporting the infection as a global health issue.

SOLUTION

MedDRA Maintenance and Support Services Organization (MSSO) has released an updated version of MedDRA 23.0 with new COVID-19 terms and revisions. The updated MedDRA dictionary will allow organizations to capture, share and analyze scientific and medical information for pre-marketing and post-marketing data. Approximately 70 new COVID-19 related terms and revisions were implemented including new High-Level Term (HLT) Coronavirus infections to group relevant COVID-19 infection terms in System Organ Class Infections (SOC) Infections and infestations.

The updated MedDRA 23.0 dictionary is now available to clients using Rave Coder.

CHALLENGE 3: MAINTAINING QUALITY AND SUPPLY

Rave RBQM

CHALLENGE

Restrictions of access to sites by staff and patients may affect the investigators' ability to maintain medical oversight. This may impact, among other key processes, completion of trial assessments, completion of trial visits, and the provision of Investigational Medicinal Products (IMPs).

*New Medidata Solution

Travel restrictions are impacting the ability of site staff and monitoring resources to perform oversight responsibilities to ensure subject safety and data quality.

*New Medidata Solution

SOLUTION

Prior to making modifications to existing risk control mechanisms and monitoring strategies a risk assessment should be performed to establish the risk to trial participants, data quality, and data efficacy. To support industry in performing risk evaluations, Medidata is offering at no charge a Risk Assessment Template* to support the development and documentation of monitoring strategies by collecting critical to quality data, mitigation strategies, and risk control mechanisms.

A revised version of the Risk Assessment Template has been created following revised regulatory guidance and can be accessed [here](#).

Rave CSA Critical* (Centralized Statistical Analytics) is a customized solution to support sponsor oversight responsibilities by incorporating next-generation analytical tools and algorithms into a quickly implemented solution (<2 weeks go-live) providing:

- Real-time data availability for proactive early data oversight
- Focused Key Risk Indicators (KRI) on areas of greatest risk
- Remote management of site processes to mitigate risk
- Detection of data patterns and anomalies
- Automated insights into subject safety, data integrity, and site performance
- Mitigation of risk due to site monitoring and patient visit disruption

These allow for increased efficiency in data review and centralization of review activities and risk/issue detection - a critical capability that can maintain and support sponsor oversight responsibilities and allow earlier access to data and enhance key decisions making capabilities.

Rave Imaging Critical*

CHALLENGE

As a result of global restrictions, most sponsors are experiencing an inability to adequately monitor their active studies on site, and may not be able to manage critical document acquisition and SDR activities. Some have turned to less secure, antiquated, risky tools to manage these critical documents such as fax, email, video and file sharing software. Without the ability to securely manage these documents, patient safety and data integrity are at risk and studies may not progress.

Regulatory guidance allows for sponsors to find ways to perform critical document management and SDR remotely via a secure cloud-based viewing portal in certain regions, excluding EMEA.

*New Medidata Solution

SOLUTION

Based on the current FDA Guidance, Medidata has tailored its Rave imaging workflow tool to enable clients to rapidly and remotely deploy a method to assist monitors in their critical document acquisition, workflow, and Source Document Review (SDR). Rave Imaging Critical is a streamlined and quick-to-implement solution (2 weeks go-live) that helps fill the gap when studies have critical timelines and no secure option to collect, de-identify, manage, review and verify critical study documents. Easy to get started with no software to download, is available at no cost to the sites, and can be used as a primary solution or alternative for sites.

Rave Imaging Critical:

- Acquires documents, via secure browser-based uploads, routes and manages document workflows to support source document review and verification remotely
- Is a 21 CFR Part 11 compliant system that includes the ability to de-identify and redact Personally Identifiable Information (PII) and Protected Health Information (PHI)
- Mitigates risk due to site monitoring and patient visit disruption for some studies with no secure option to manage critical documents

Rave EDC and Rave RTSM

CHALLENGE

Patients can't get to the site for dispensation but the site is open.

Patients can't get to the site for dispensation - sites are open but do not have supply for dispensation.

Sites are closed and patients need a dispensation.

SOLUTION

Sites can process dispensation through Rave EDC as a visit and send the drug to the subject via a courier. Rave EDC could be updated to store the courier tracking number (collected as text data). Adding a new field would require a migration in Rave EDC.

There are several options to have drug sent to the patient from the depot or a central pharmacy. In Rave RTSM (randomization and trial supply management), the subject has to exist at the site where the drug supply is located. There are several options we are executing to manage transferring subjects and creating dummy shipments to allow a shipment to be sent to the patient's home from a location other than the site. We're able to work with study teams to help set up the best option based on the study design and logistic considerations.

Some of the methods above can also be used to allow a direct to patient shipment when the site is closed. Alternately, subjects may be transferred to sites that are open. We have a "How-to" procedure ready to share with you.

CHALLENGE

Subjects are able to have an onsite visit but future visits are questionable.

Supply chain concerns make sites want to have more buffer stock on hand or less (depending on if the concern is availability of drug or availability of shipments).

SOLUTION

Multiple dispensing visits can be made in Rave EDC at the same time, providing additional IMP for the subject. If this will become standard, DND dates should be updated so that the drug does not expire over the longer time period between dispensations. Our Services team can provide specific steps that can be utilized to ensure off-cycle/unscheduled visits can be conducted without issue.

Supply plans can be instantly adjusted by end users to meet the changing needs of individual study sites. To ensure that the site is stocked with additional drug to service a larger number of visits, the maximum buffer can be increased or the long window extended. Alternatively, a supply plan can also be adjusted to maintain less inventory by shortening the long window or reducing the maximum buffer. The site can also be deactivated for shipping in the case of a closed site or dispensations occurring from alternate sites.

CHALLENGE 4: ACCELERATING STUDY START-UP

Rave Grants Manager COVID IIS*

CHALLENGE

Budgeting for the investigator-initiated studies (IIS) is different from a normal trial. IIS trial budgets are typically built as small cost buckets, with the Sites (not the Sponsor) indicating what the costs are and what they want the Sponsor to pay. This approach causes delays in getting approval with the Sponsor as a more granular activity level budget is needed. The Sponsor will also need reliable data to verify if the costs are fair.

With COVID-19 investigator-initiated studies, there are budget negotiation delays due to the gap between the Site's and Sponsor's individual cost benchmarks. Disparate data sources for clinical procedure activities and other direct costs at the investigator and site-level can undermine decision-making. There is a need for an independent industry benchmark.

SOLUTION

Medidata has developed a COVID19 vaccination study budgeting solution, **Rave Grants Manager COVID IIS**, to help investigator-initiated studies develop detailed trial budgets for patient, procedure and site costs. Leveraging Medidata's deep fair market value data and our clinical trial budgeting expertise, Sponsors can streamline the budget build process for their sites.

Rave Grants Manager COVID IIS enables Sponsors to negotiate investigator-initiated studies quickly using a single, reliable fair market value data source as well as a complexity analyzer. The complexity analyzer calculates benchmarks with industry averages, along with a site's work effort required by the procedures, visits and protocol. This helps sponsors determine fair site payments based on relative study complexity.

CHALLENGE

**Compliance and auditing risks.
Lack of internal COVID-19 related
data to establish FMV to ensure
Sponsors are not overpaying or
underpaying sites.**

*** New Medidata Solution**

SOLUTION

Medidata's deep fair market value data provides auditable defensible rates. An audit trail of negotiation activity is retained for reference and compliance with fair market value regulations.

Rave EDC and Rave RTSM

CHALLENGE

**COVID studies need to be up and
running quickly.**

SOLUTION

Rave RTSM with basic EDC forms can be up and running in as little as two weeks for a randomization only study and as little as three weeks with basic trial supply management. We recently had a COVID study go from kick-off to UAT in 12 days with randomization and trial supply management.

Summary

Medidata's commitment to supporting the life sciences community is unwavering. We will continue to monitor the impact of the virus on clinical studies, and provide updated information as available. We are working hand-in-glove with our sponsors and partners to identify issues caused by the pandemic and to find innovative ways to support you with solutions, technology and advanced analytics. From operations to oversight, from supply management to synthetic control arms, from virtualization to centralization of data oversight, we are committed to helping you continue your clinical research.

In this environment of uncertainty and anxiety, what is certain is Medidata's commitment to our mission, we exist to Conquer Diseases together.

About Medidata

Medidata is leading the digital transformation of life sciences, creating hope for millions of patients. Medidata helps generate the evidence and insights to help pharmaceutical, biotech, medical device and diagnostics companies, and academic researchers accelerate value, minimize risk, and optimize outcomes. More than one million registered users across 1,700 customers and partners access the world's most-used platform for clinical development, commercial, and real-world data. Medidata, a Dassault Systèmes company (Euronext Paris: #13065, DSY.PA), is headquartered in New York City and has offices around the world to meet the needs of its customers. Discover more at www.medidata.com and follow us [@medidata](https://twitter.com/medidata). The Operating System for Life Sciences™.

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