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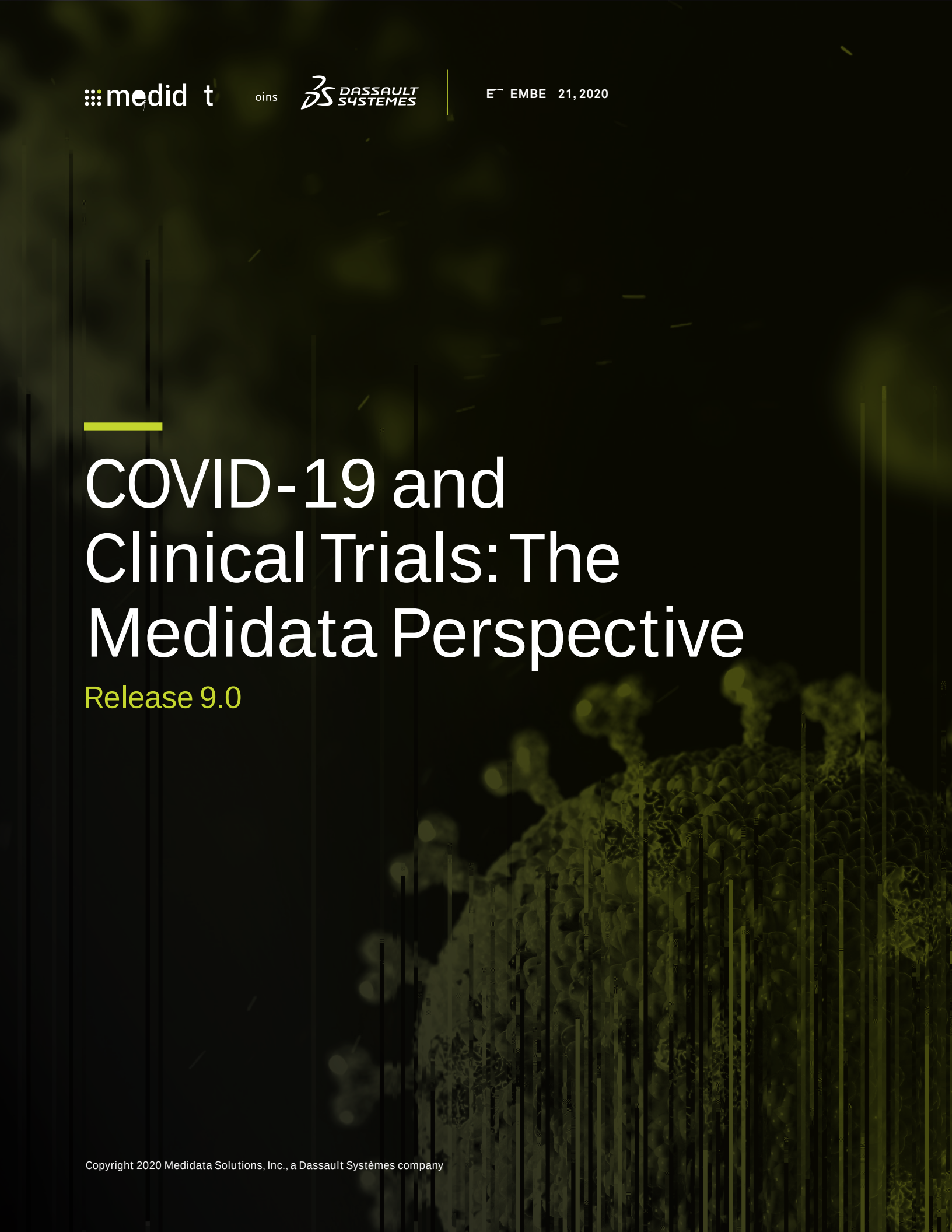
COVID-19 and Clinical Trials: The Medidata Perspective

Release 9.0



What's New/What's Signi□cantly Updated in Release 9.0

- Updated: Metrics on new patients entering trials by country/region and therapeutic area by month
- Updated: Regulatory Response
- Updated and New: Ongoing Impact to Medidata Customers, Patients and Trials - Results of 2nd Site Survey on Impact of COVID-19 to Sites
- Updated: Discovering a Vaccine
- Updated: Summary Table of the current vaccine clinical trials for COVID-19
- Updated: Graphical Representation of COVID-19 Vaccination Trials
- Updated: New and Adapted Medidata Solutions to Assist Sponsors/CROs and Patients in Mitigating the Impact of the COVID-19 Pandemic on their Clinical Trials
- Updated: Summary

Insights to Ongoing Data Capture in Clinical Trials

Medidata is continuously monitoring the global impact of COVID-19 on clinical trials. Our □rst data and insights impact report was released on March 23, with subsequent releases on April 3, April 17, May 4, May 18, June 15, July 13, August 12 and now September 11. At the beginning of the pandemic, we were looking at year-over-year changes to understand and grasp the magnitude of COVID-19 on the impact on clinical trials in terms of trial activity, across geographies and therapeutic areas (TAs). As reported in Release 6.0, we had started to see a leveling off of the impact and regional □uctuations. After we aggregated several months of data, we pivoted to help the industry better understand the changes over time at the geographic and TA level, and enable real-time decision making.

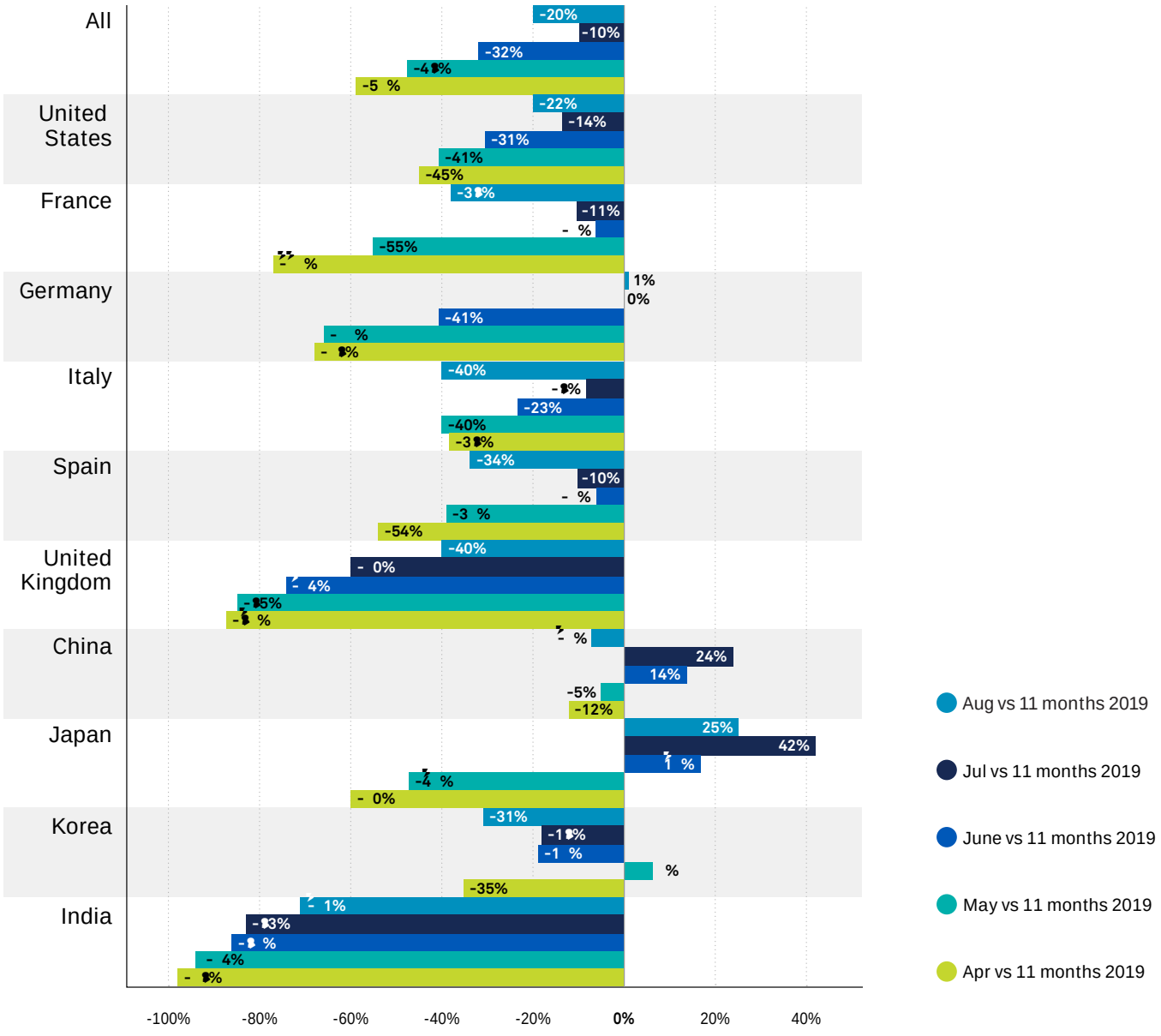
Our data and methodology continues to be improved over time, and as such there may be some variability from report to report. Overall trends, however, remain the same. Below, you can □nd an updated analysis of trial activity as measured by the average number of new patients entering trials per study-site. As we mentioned in our last release, the negative effects of COVID-19 on new patients entering study-sites are likely understated as we are looking at trials that are still actively recruiting patients. We expect COVID-19 to continue to impact trials, at different times and with varying force across the globe. With that in mind, we will continue to highlight insights from Medidata's cross-industry data. This analysis included 5,222 studies, 198,120 study-sites.

Globally, we saw a decline in new patients entering trials per study-site at the end of August, at -20% of pre-COVID baseline, as compared to about -10% for July. Recovery continues to 20 (5 (ooking a)7r1dy-s)m (om)10.1 c t, at -20% ow5 (e)5 (5 (el)-200% udy-s

Globally, from a therapeutic area (TA) perspective the impact has varied as well, with most TAs experiencing a downturn in August, including Oncology - similarly to what we saw in the U.S. Cardiovascular, however, saw an improvement in August, moving from -49% in July to -20% in August as compared to its pre-COVID baseline. Overall, non-oncology TAs are at -31% of their pre-COVID 2019 baseline.

The differing impact on TAs and geographic regions, as well as the continued fluctuations, underscore the need to continue to track impact real-time at a granular level, so that we can enable companies to make the best decisions on when and where to focus efforts, help them continue to run their trials and get treatments to patients. See Figure 2 for more details.

Figure 1: Change in weekly patient starts in tested studies by region



F gu e 2: Cha ge e at e ts e te g stud -s tes A

Regulatory Response

Over the past months multiple authorities, including those below, have issued emergency guidance on trial conduct amidst COVID-19. Technology enablement topics including those in Figure 3 and many other topics including protocol deviation management, investigational product handling, protocol amendments, ethics committee review, etc. are common areas of

Frequently discussed topics include telemedicine/decentralization (see FDA Question 20), consent and eConsent (See FDA FAQ 10 and 11), expectations on electronic records/ signatures rules (See FDA FAQ 24), and remote monitoring including remote source data veri□cation (rSDV) (See Question 14). Note that while the US FDA, UK MHRA, Australia DoH, Health Canada, and Singapore HSA suggest rSDV is possible, the EMA leaves it as an option in very limited circumstances (Section 11 and Annex) and some outright discourage it including Germany and France. Centralized monitoring activities are suggested by most regulators, however.

The regulatory appetite for making COVID □exibilities extend beyond the pandemic is uncertain but there is reason to believe change is possible. For instance, US FDA Commissioner Hahn's June 1 remarks, "The COVID-19 Pandemic - Finding Solutions, Applying Lessons Learned," indicated a desire to make some of the changes, (i.e., accelerated receptiveness to trial decentralization, master protocols, real world evidence) endure beyond the pandemic. Additional information may be found in Medidata's regulatory blog.

Ongoing Impact to Medidata Customers, Patients and Trials

COVID-19 SITE SURVEY 1.0 - APRIL 2020

The impact of the pandemic on sites was well documented by a survey of over 1,000 clinical site personnel performed by Medidata in late April 2020. Not unexpectedly, the survey results clearly and dramatically show that most sites are feeling the negative impact of the pandemic on current and future trials, speci□cally around delays in patient enrollment and recruitment. They also are concerned about the impact of trial delays and cancellations on their □nancial 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 □exibility 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. The detailed results of the survey can be reviewed here.

COVID-19 SITE SURVEY 2.0 - AUGUST 2020

A follow up survey of sites was sent to over 7,000 sites during the □rst week of August 2020. Preliminary results of the 734 respondents indicate that sites are coping better with the pandemic now than when we surveyed them in April. Slightly over half

Figure 4: Impact of COVID-19 on Digitals

We once again asked sites to tell us how COVID-19 was impacted speci□c activities within their trial with 5 being severely impacted and 1 being not impacted at all. Generally, the results across all activities were better than what was reported in April with no weighted average results for any activity being moderately or severely impacted by COVID-19. The highest weighted averages for the impact of COVID-19 on ongoing trials were for the sites' ability to recruit patients (3.02) and enroll patients (3.02) and the increasing costs of personal protective equipment (a new question in this survey) was 2.87. The full results can be seen in Figure 6.

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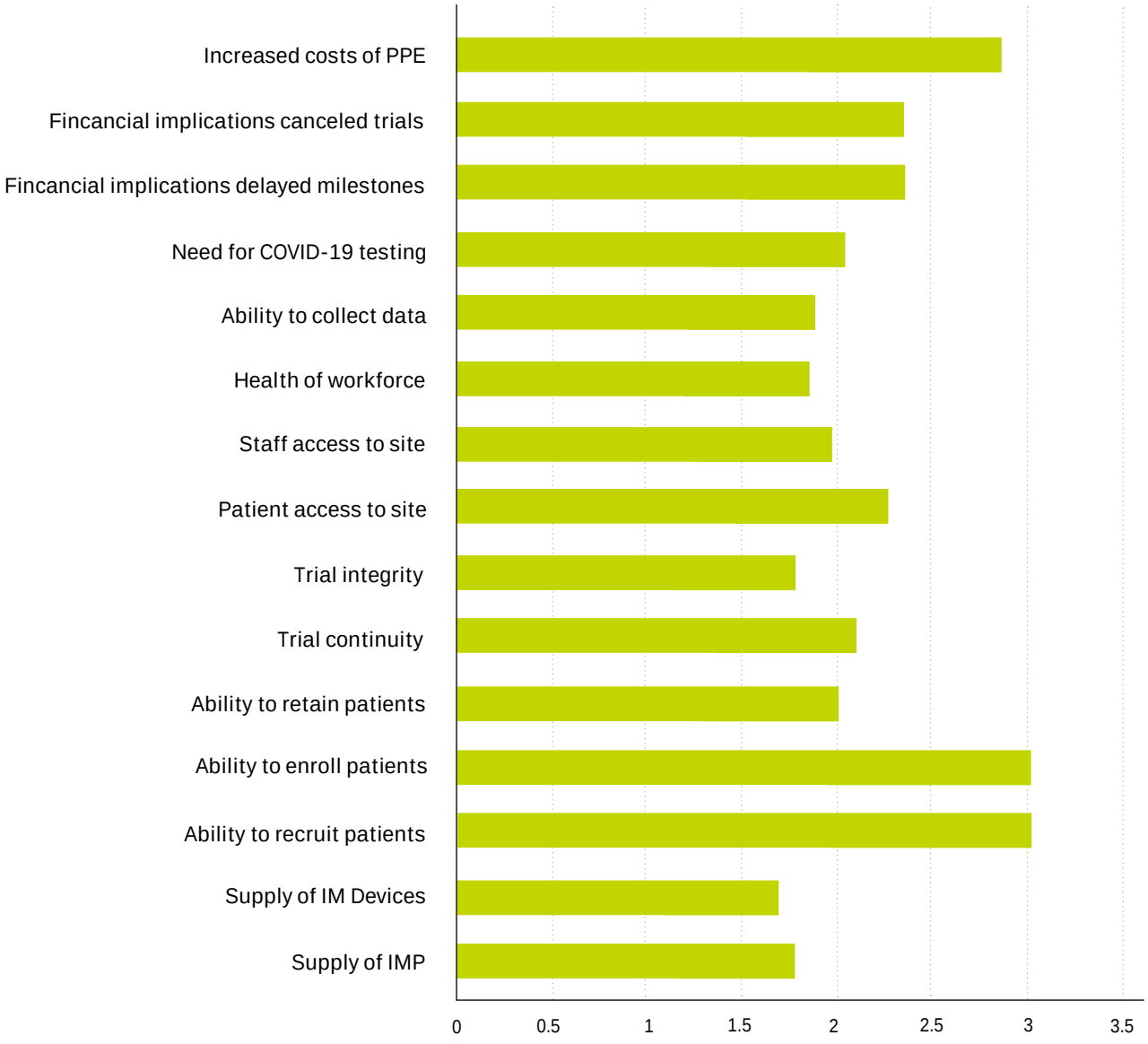


We also reasked the sites about how and when they would be responding to the impact of the pandemic on the trials. When looking at the results for activities that sites had already done, about 40% of respondents had implemented study protocol amendments, had halted recruitment for ongoing trials and 40% had switched patient visits to virtual. Of note, about one-third of respondents indicated that they had delayed a study and/or had extended patient visit windows. About one-fth of sites test patients for active COVID infection but only about 10% test for past infection. See complete results in Figure 7.

In this survey we asked site respondents to think ahead 6 months and tell us how they would characterize their feelings about the future of their clinical trials with 5 being highly optimistic and 1 being highly pessimistic. The weighted average of the responses was 3.67 with almost 60% of sites being optimistic, while only 16.5% were pessimistic. See Figure 8..

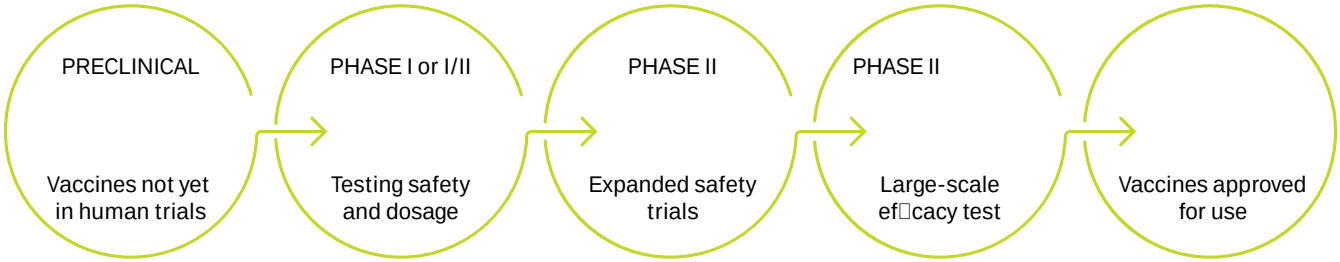
Figure 8: Feelings about the future of clinical trials

More detailed results of Medidata's second site survey will be published in the next month.

From the patient's perspective, a survey of its Phase III patients by a Canadian CRO found that amid the changes COVID-19 has brought to its sites, patients were still committed to continuing their trials. When asked how the CRO could further support its patients, many mentioned medication deliveries and the option to have study visits in traditional, virtual, and hybrid forms, but what was most important was "someone asking us if we are okay."

There were a variety of different ways patients wanted to stay engaged – updates on COVID-19, updates on their research

Figure 9: The COVID-19 vaccines clinical development



New and Adapted Medidata Solutions to Assist Sponsors/CROs and Patients in Mitigating the Impact of the COVID-19 Pandemic on their Clinical Trials

The following tables provide details about the Medidata's solutions available to assist with COVID-19-realted clinical 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

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de sta d g the ou t /s te/ d sease a ea a ct a coss the dust , a d develo g sk t gat o a d e ove la s.	al l a ct A al t s: COVID-19 tracking and forecasting powered by 6,000 active and 20,000 overall industry trials eal- e tuat o a k g: iInform critical decisions on where to focus efforts by benchmarking impact of COVID-19 on own trials vs. industry • Assess impact of COVID-19 through standard dashboards • Understand weekly and monthly trends, and YoY performance • Views at portfolio, study, country / region and site level l a ct Fo e ast g: Plan ahead by understanding leading indicators of slowdown and recovery at a country and site level • Track performance at country and site level to understand which countries, sites are coming back on-line • Overlay trends in COVID-19 testing and infection rates with impact on trials to identify leading indicators of recovery at a country / region / site level

CHALLENGE 2: RECONSIDERING TRIAL DESIGN TO ENABLE DATA CAPTURE

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ov de a s fo ssed o sked v s t fo s to e e otel lled out at e ts o e st stud es.	Medidata's eCOA solution can be used to convert site-based data forms to remote data forms. If study modi cations 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. Learn more about Rave eCOA here

Med data/

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ua t f the a ct of t al a t a ts th C ID-19 s to s o o go esea ch stud es.	In late April, Medidata and 3DS launched the COVID-19 Symptom Tracker as part of myMedidata (the Medidata Patient Portal), which will 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.

A co Al thet cCo t ol Data base / al Des g

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I ov g u de sta d g of safet e e e tal t eat e ts (e.g., chlo oqu e) that a e o u de ev e fo coss- d at o use.	Support research by providing aggregated data, e.g., Synthetic Control Database (SCD) to enhance understanding of expected and unexpected AEs for products being studied for COVID-19. These drugs are already marketed with a mature safety pro le, 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 con dence and validation in trial design, better understand inclusivity of patients populations to better re ect real world clinical practice, and potentially decrease sample size requirements for event-driven trials.
Clos g out o go g stud es g ve ba e s co let g v s ts.	Leveraging historical clinical trial data to augment or replace control arms of trials that are in danger of high dropout or unful lled enrollment due to COVID-19; reduce scienti c uncertainty the advantage to the next phase. Reduce patient enrollment burden or increase statistical power.

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CHALLENGE 3: MAINTAINING QUALITY AND SUPPLY

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at e ts a 't get to the s te fo d s e sat o but the s te s a e .	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 eld would require a migration in Rave EDC.
tes a e osed a d at e ts eed a d s e sat o .	Subjects may be transferred to sites that are open, or if site users are able to work remotely they can register a visit in Rave EDC that is con gured in RTSM to be Direct to Patient and have the dispensed items shipped from the Depot to the patient's home.
u e ts a e a le to have a o s te v s t ut futu e v s ts a e quest o a le.	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 speci c steps that can be utilized to ensure off-cycle/unscheduled visits can be conducted without issue.
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CHALLENGE 4: ACCELERATING STUDY START‐UP

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th C ID-19 vest gato - t ated stud es, the e a e budget egot at o dela s due to the ga bet ee the s te's a d s o so 's d v dual ost be ch a ks. he e s a eed fo a de e de t dust be ch a k.	ave G a ts Ma age C ID II enables Sponsors to obtain a grant budget that allows them 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.
Co l a ea d aud t g sks. La k of te al C ID-19 elated data to esta bl sh FM to e su e s o so s a e ot ove a g o u de a g s tes.	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.

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Summary

All eyes are now on the COVID-19 vaccines in Phase 3 of trials. In an unprecedented and historic move 9 biopharma companies pledged to follow only the science in seeking approval. And the CEO of Pfizer communicated they will know about the safety and efficacy of their vaccine by the end of October. Regulatory bodies like the CDC are predicting longer timelines, likelier second or third quarter of 2021. And we see continued and increased investment in vaccine development; just in the last few days Germany announced an increase in funding.

The politicization of the clinical trial process has increased and is an ongoing cause of concern. And as those processes progress and move downstream other issues are bubbling to the surface. There's more discussion and planning for manufacturing and the infrastructure required for universal vaccine distribution. With that progress comes more issues; we are seeing vaccine hesitancy at a high level, even as high as 50% in the US according to polling.

Globally we are watching countries balance a return to normal while managing ongoing outbreaks. Restrictions are lifted, cases rise and restrictions are reimposed. In the U.S. cases continue to rise in all regions outside of the Northeast, and the anti-mask contingency is troubling. And across the globe testing at scale continues to present challenges; in the UK limitations on test processing are significant. The opportunity to use the lockdown period to upscale testing, tracing and treatment has been unevenly applied across countries. Rapid, reliable instant testing is the goal yet to be achieved.

In positive news, sponsors and sites continue to adapt to the new normal that COVID-19 has imposed. COVID-19 is enabling - actually, forcing - aspects of clinical trial management that have been in discussion for decades.

We will continue to monitor and share updates for the duration, and our support of our customers and partners in unwavering.

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 **. ed data. ** and follow us **@ ed data**, The Operating System for Life Sciences™.

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