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Digitalized Adaptation of Oncology Trials during and after COVID-19

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While the global scientific community is actively developing therapeutics and vaccines for COVID-19, healthcare services and translational research of other “non-urgent” illnesses have been shelved (Leford, 2020). The sudden pause has brought inevitable changes or delays in cancer treatment (Upadhyaya et al., 2020) and increased COVID-19-related mortality in cancer patients (Mehta et al., 2020). These impacts on cancer research and clinical practice could be far-reaching post-pandemic (Colbert et al., 2020) unless current modes of clinical trials are re-evaluated and contingency measures are proactively planned.

China observed the first wave of the COVID-19 outbreak, providing a panorama of epidemic and responses throughout different phases. When COVID-19 first hit China, various digital solutions were introduced, such as artificial-intelligence-powered CT imaging tools (Zhang et al., 2020) and individual tracing systems. Later on, smartphone-based “health codes” were applied nationwide as health permits. Telemedicine, empowered by 5G technology and the Internet of things, quickly alleviated the closures of outpatient services. Clinical trials in China encountered disruptions in February, when active COVID-19 cases surged, followed by a rebound after March (Medidata, 2020). To quantify the dynamic impacts of COVID-19 on cancer trials and assess the involvement of digital solutions in China’s adaptation, two serial cross-sectional investigations were conducted between February and May from the viewpoints of hospitals and the pharmaceutical industry (Figures S1A and S1B and Table S1A).

In February, 45.1% (221/489) of ongoing clinical oncology studies were delayed, while 33.5% (164/489) were forced to change protocols (Figure S1C). Nearly 90% of cancer hospitals suspended new trials completely or partially (Figure S1D). Similar impacts have also been observed in trials of other illnesses (Figure S1C). The disturbance arose largely from limitations in follow-up visits, patient enrollment, and personnel’s hospital access (Table S1A). The degree of impact predominately correlated with the epidemic severity. For example, Hubei province, where the city of Wuhan is, suspended all clinical trials other than for COVID-19.

To mitigate, hospitals and sponsors reported technology-based adaptation measures to overcome operational challenges and ensure participants’ safety. More than 65% of the study sites transformed ethics committee reviews into an online mode (Figure S1D), which was almost absent pre-pandemic. With regards to trial implementation, frequently adopted approaches included remote visits, teleconference, drug delivery to patients, centralized monitoring, and electronic patient-reported outcomes (ePROs) (Figure S1E).

In response to the interrupted follow-up visits, which were mostly affected by COVID-19 (Table S1A), most respondents conducted remote or virtual visits (Figure S1G). Disease characteristics, drug administration route, and facilities-based disease assessment were major considerations when determining the feasibility of remote visits. For instance, 48.9% of visits were performed remotely for an oral hypoglycemic drug at 22 sites, while none were conducted for a breast cancer drug requiring intravenous delivery at 19 sites, associated with 44.2% uncompleted visits in the month of February (Figure S1F). In terms of restoring other disrupted processes, centralized monitoring realized efficient remote data verification (Figure S1G), exemplified by the digital monitoring system used in at least 150 cancer studies in Peking University Cancer Hospital. eConsent, ePRO, and wearable devices were deployed to allow the continuation of new enrollment and timely data entry (Figure S1G).

Furthermore, the blockchain technology facilitated accurate tracking of direct medication delivery to patients (Ting et al., 2020).

As the COVID-19 epidemic subsided in China, disruptions of clinical trials were gradually resolved. New cancer studies were allowed to initiate gradually (Figure S1D). More ongoing trials continued according to protocols and even resumed at pre-pandemic pace (Figure S1C), associated with fewer out-of-window visits (Figure S1F). Global disruptions of clinical trials in April and May were similar to those in China in February (Medidata, 2020). Virtual visits and direct-to-patient drug delivery were reported in equivalent proportions between our findings and the results from the global survey (Medidata, 2020). Notably, a large portion of respondents planned the implementation of digital solutions if the pandemic were to continue.
In retrospect, this unexpected crisis definitely accelerated the deployment of digital health trials worldwide (Upadhaya et al., 2020). The new modes adopted during the pandemic call for further investigation to explore effective ways of translating digital tools into practice and regulating them in the fast-evolving digital era. Implementation of contingency measures largely relied on the pre-existing digital infrastructures. Pre-pandemic experiences with the ePRO system were associated with significantly more usage of ePRO during the pandemic, as was the case for wearable devices (Table S1B). Future integration of multiple functions into one platform can enable seamless and efficient implementation, robust to interferences by future unexpected circumstances like COVID-19.

Given the rapidly evolving technological landscape, updated regulatory frameworks are required to detail the standards of procedures and application scenarios. The Clinical Trial Transformation initiative, co-founded by the U.S. FDA and Duke University, has facilitated the switch to virtual visits using digital solutions amid COVID-19. In China, a guidance detailing the scopes and contents of digital health trials is under development. When it comes to regulatory acceptability, benefit-risk assessment needs to be evaluated comprehensively when using digital tools, including the relevance of endpoint outcomes, validity, and compliance (Cerreta et al., 2020).

Digital technologies have fulfilled the needs of cancer trial adaptation to this pandemic. However, some adjustments were expedients, such as reduced on-site visits and de-escalated anticancer regimens (Upadhaya et al., 2020). These inevitable deviations or violations may introduce bias in interpretation of results and uncertainties in regulatory decision making. The FDA has thus issued statistical recommendations to mitigate the impacts on meeting trial objectives. To counteract this, lessons learned regarding broader adoption of digital health trials and pre-planned contingency plans with digital adapatation approaches can be exploited to ensure trial continuity and data integrity in future crises.

SUPPLEMENTAL INFORMATION
Supplemental Information can be found online at https://doi.org/10.1016/j.ccell.2020.06.018.

DECLARATION OF INTERESTS
T.W. is the managing director of DIA Greater China and senior vice president of DIA Global. T.C. is a senior manager of DIA China. Y.L. is the general manager and J.C. is the director of quality assurance of LinkStart. The other authors declare no competing interests.

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