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Drug development process and COVID-19 pandemic: Flourishing era of outsourcing

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Abstract:

Traditional drug development is a tedious process with involvement of enormous cost and a high attrition rate. Outsourcing drug development services to contract research organizations (CROs) has become an important strategy for cost and risk reduction, capacity building, and data generation. The therapeutic and operational expertise of these CROs has allowed pharmaceutical industry to reduce in-house infrastructure as well as research capacity. Working with specialized CROs has not only increased the rate of success but also the speed of drug discovery process. Small firms with promising molecules but limited resources and large firms interested in diversifying their dimensions are utilizing the services of efficient CROs. Globally, approximately one-third of the drug development processes are now being outsourced and the data generated by the independent third party are well appreciated during regulatory submissions. In this article, we discuss the international and national trends, outsourcing services and models, key considerations while selecting CRO, and benefits and challenges of outsourcing. Further, we discuss how the technical expertise of competent CROs was utilized when traditional ways of conducting clinical trials were disrupted by the COVID-19 pandemic. Taken together, the increasing health-care demands, COVID-19 pandemic or any other such upcoming health crisis, and recent advances in advanced technologies (machine learning and artificial intelligence, etc.) are likely to fuel global CRO market in the coming years.

Keywords:

Artificial intelligence, contract research organizations, COVID-19, drug development, outsourcing

Introduction

Development of a new compound from basic research to market approval is a herculean task taking decades of research and development (R&D) and costing approximately 0.3–2.8 billion USD.^[1] Merely 12% of the drug candidates reaching clinical trial stages get the US Food and Drug Administration (FDA) approval, thus implicating huge monetary risk for pharmaceutical and biotechnology industries.^[2] The cost of new drug development is influenced by many factors

including cost of discovering new targets and their preclinical development, cost of clinical trials, cost of product profile, and many more.^[3] Introduction of advanced genomics and proteomics techniques has revolutionized the drug discovery process by facilitating identification of newer drug targets. At the same time, maintaining state-of-the-art facilities and retaining specialized actors of the field under one roof is challenging for the stakeholders.^[4] Therefore, to reduce the R&D cost and accelerate drug development process, the small and large biopharmaceutical industries (sponsors) are aggressively moving forward to get their work outsourced through contract research organizations (CROs).

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In the early 1950s, Charles River Laboratories and Huntingdon Life Sciences were among the first CROs to offer various preclinical experimental services. The CROs flourished later in the 1980s, when stringent regulatory frameworks were laid down by different government agencies for regulating clinical trials and approval of new drugs. During this phase, CROs such as Quintiles, Parexel, and Pharmaceutical Product Development (PPD) entered into clinical trials and related operation market. As of now, there are more than 1000 CROs working globally, handling different aspects of drug development and commercialization.^[5]

International and National Trends of Outsourcing Market

Globally, the CRO market is forecasted to grow from 38.4 billion USD in the year 2018 to 90.9 billion USD by the year 2026 with a compounded annual growth rate (CAGR) of 11.4% during the 2019–2026 period.^[6] Increasing health-care demands, costly drug development process, and steep rise in noncommunicable diseases including cancers are likely to fuel the global CRO business in coming years. In terms of different services provided, clinical CROs are forecasted to own more than 50% of the market share, whereas services such as drug discovery, laboratory services, and preclinical evaluation platforms will share the remaining outsourcing market. Further, due to rising cancer cases along with the growing demands of effective treatment therapies, oncology segment predominated among other therapeutic areas in 2018.^[6] Geographically, North America holds the highest market share of CROs followed by Europe, Asia Pacific region, and the rest of the world. The market in Asia Pacific region is likely to expand because of diverse population, availability of skilled health-care professionals, and large patient pool of communicable and noncommunicable diseases.^[7]

As per national market research report, the CRO industry in India is expected to double from 0.95 billion USD in the year 2020 to 1.8 billion USD in the year 2027. This CAGR of 10.8% is attributed to blooming oncology research, blossoming biopharmaceutical sector and changes in drugs and clinical trial rules by the Indian government.^[8] In addition, the pharmaceutical sector attracted the Foreign Direct Investment of 17.99 billion USD in the last 21 years (April 2000–March 2021), with a significant rise from 0.26 billion USD in 2018–19 to 1.49 billion USD in 2020–21.^[9] Further, the restrictions of conducting more than three clinical trials at one time have also been lifted by the government as per New Drugs and Clinical Trials Rules 2019. Furthermore, the timeline of decision to conduct clinical trial has been reduced to 90 days for global clinical trial and 30 days for national clinical trial, which use to take up to 6 months

previously.^[10] These reforms will improve clinical research in India, which currently holds only 1.2% of the global clinical trials^[11] despite huge disease burden and large patient pool and will, therefore, provide a fertile ground for CROs to flourish.

Outsourcing Services

Based on the services provided, CROs are broadly classified into preclinical and clinical categories. Preclinical CROs test the compound or devices at the initial stages of their development. They perform a wide range of functions from synthesizing/manufacturing the compounds or devices, running various complex chemical and analytical assays for screening, and conducting *in vivo* animal experiments for efficacy and toxicological studies. Rapidly evolving technologies in cell-based and gene-based therapies require advanced well-equipped laboratories to synthesize and validate the compounds with high efficiency, accuracy, and precision. Developing and retaining such in-house facilities with specialized research personnel poses a huge economic burden for the sponsors in addition to the uncertain success potential. However, CROs, equipped with high-end technologies and expert scientific workforce, not only reduce the time for preclinical drug development but also help the sponsors in adopting “fail-fast” approach by screening and recognizing the potential pitfalls at an early stage.

Clinical CROs focus on services ranging from planning and execution of clinical trials to postmarket surveillance including handling different phases of clinical trials, medical writing, data management, regulatory and medical affairs, and pharmacovigilance. Stringent dynamic regulatory requirements to file Investigational New Drug and New Drug Application can be handled by experienced regulatory domains of CROs. This can reduce the time to enter the market, as many new drug applications fail owing to deficiency in providing appropriate substantial evidence for proposed indication, thereby delaying approval process leading to loss of revenue for the sponsor.^[12]

Pharmaceutical and biotech companies are increasingly outsourcing the research activities to CROs. These activities range from basic research including *in vitro* and *in vivo* models to late-stage clinical development. For instance, AstraZeneca collaborated with IQVIA (Operation Warp Speed) to speed up clinical studies for assessing potential efficacy of AstraZeneca’s COVID-19 vaccine using IQVIA’s Virtual Trial solutions platform.^[13] Covance and Novartis collaborated to accelerate the development of clinical data warehouse designed for supporting data integration and conduct of meta-analysis for preclinical and clinical studies.^[14] The relationship of Parexel with

Pfizer is evolving from vendor to becoming a strategic partner. Pfizer collaborated with Parexel for clinical trial outsourcing using different outsourcing models ranging from full-service approach to functional service provider.^[15]

Additionally, sponsors collaborate with academic institutions for various research activities including early phase of drug development. For instance COVID-19 vaccine was developed by Oxford, and the marketing rights were taken by AstraZeneca. This collaboration brought together the expertise of vaccine development unit of Oxford and industrial capabilities of AstraZeneca with respect to development and commercialization. In the early 2018, Novartis collaborated with Harvard University and Medical School to develop implantable and injectable systems that can boost immune response in different types of cancers. Amgen collaborated with University of Iceland to study genome-wide association studies to find genetic variations in human genome responsible for high risk of certain diseases. Roche partnered with various academic institutions to create screening methods for autism spectrum disorders.^[16]

Outsourcing Models

Strategies for outsourcing activities may vary from sponsor to sponsor. Few sponsors may prefer to outsource their work among different CROs whereas others may prefer to avail a wide range of integrated services from a single CRO, A One Stop Shop". Many sponsors also go for hybrid approaches, wherein few services are utilized for one and complete services are outsourced for another project. Flexibility in outsourcing can be built on a predefined agreement between CRO and sponsor.^[17] The most commonly used models [Figure 1] for outsourcing R&D activities are discussed below:

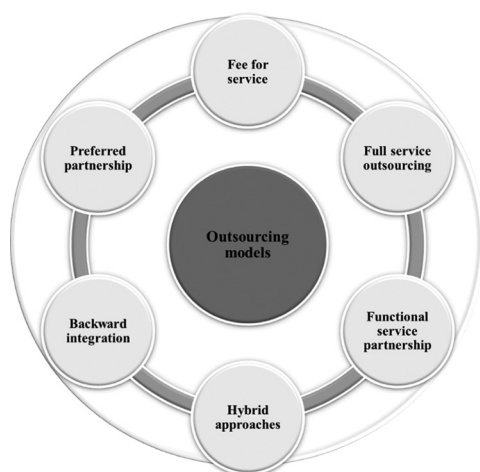


Figure 1: Different outsourcing business models adopted in pharmaceutical industry

Fee-for-service outsourcing

This approach is useful where a task is to be outsourced on the basis of predetermined fee, for example, screening a number of compounds by running various assays, management of clinical trials, synthesizing reference compounds, etc.^[17]

Full-service outsourcing (FSO)

This model is usually used by a newer/smaller firm, who has just developed or synthesized a new compound with good therapeutic potential, but does not have technical expertise required for further developmental process.^[18]

Functional service partnership such as full-time employee-based engagements (FTE)

In this model, the staff of CROs is fully dedicated to the sponsor to carry out the particular functions for a single project or multiple projects. This approach provides flexibility and increases efficiency toward multiple projects by hiring a team of experts from CRO.^[17,18]

Preferred partnership

Big international biopharmaceutical companies partner preferably with international CROs of high repute such as IQVIA and Parexel which either offer full service or functional service partnership model. For example, Merck outsourced all their laboratory work globally to Coax.^[19]

Backward integration

Under this model, CROs invest in small pharma or biotech companies, and in turn utilize their services such as clinical trials or other process in later stages for other projects.^[19]

Hybrid approaches

In the fast-paced environment and rapidly developing pharma-biotech sector, companies are not limited to just one model. They incorporate different approaches such as FSO and FTE to carry out required functions.^[18]

Traditionally, CROs were just helping hands for the sponsors to innovate on behalf of the clients, but the intellectual property rights remained with the sponsors. However, nowadays, as CROs are taking larger complex roles, it has become difficult to delineate the biopharmaceutical companies from CROs. For instance, some service providers have their own internal drug discovery unit with a plan to license deal with large biopharmaceutical companies for further development. To accomplish this deal, newer models such as risk sharing, royalty payments, and joint ownership of IP rights are emerging wherein the initial innovation comes from the CRO, who then collaborates with pharmaceutical companies.^[17]

To further compensate the revenue losses due to expensive drug development and approaching patent cliff, merger and acquisition (M&A) models have picked up the pace to fill R&D gap and foster innovation to attain topline growth. The small- or mid-size innovator firms with a battery of potential new drug candidates often get merged or are acquired by big biopharmaceuticals to attain financial and operational gains. The major driving force for M&A is the ongoing patent cliff causing tremendous loss of revenues. For instance, the top 25 drug developers were expected to lose approximately 85 billion USD in the period of 2019–2021.^[20] Additionally, the pharma companies also acquire generic drug makers, such as AbbVie acquired Allergan in a deal of 63 billion USD due to patent expiry of its top-selling drug Humira in 2018.^[21] In the last 5 years, approximately 2900 deals worth 1 trillion USD happened majorly in the fields of immuno-oncology, gene therapy, orphan drugs, and microbiota.^[22] Few examples of big M&A deals in the year 2021 include acquisition of Vifor Pharma worth 11.7 billion USD by Australian-based company CSL limited for pipeline drugs in the therapeutic areas of cardiorenal and iron deficiency diseases.^[23] Merck acquired Acceleron Pharma for 11.5 billion USD. Jazz Pharma merged and acquired GW Pharmaceuticals at a deal of 7.2 billion USD. Sanofi acquired Translate Bio, expert in the field of messenger RNA (mRNA), for 3.2 billion USD and acquired a small company, Tidal Therapeutics, having expertise in developing nanoparticles to deliver mRNA. Sanofi is now establishing its mRNA Center of Excellence in the United States and France.^[24,25]

Further, in today's scenario, where digital innovations are at the forefront of drug discovery and clinical trials, drug manufactures are now looking to collaborate with organizations having expertise in information technology domain. Keeping the increasing demand of computational technology, CROs have successfully expanded their domains in the areas of artificial intelligence (AI), machine learning (ML), and data analytics.^[26] There are many AI vendors offering services in drug discovery such as Insilico Medicine, BenevolentAI, Recursion Pharma, Exscientia, and Sensyne Health. Recently, in 2020, various big pharmaceutical companies have partnered with AI vendors.^[27] For instance, Pfizer collaborated with Insilico Medicine to identify potential drug targets and biomarkers through ML platforms. Takeda collaborated with Recursion Pharma for preclinical and clinical evaluations of various candidates. Similarly, Bristol-Myers Squibb collaborated with Sensyne Health's ML platform to conduct research for myeloproliferative neoplasms.

Key Considerations for Outsourcing

Sponsors select CRO services based on their unique

selling proposition including strong reputation, technical competency, understanding of regulatory framework, expertise in particular therapeutic areas, ability to complete task under predefined timelines, producing high-quality data, and cost-effectiveness [Figure 2].^[28] In the following section, we have discussed some important key aspects in selecting a CRO.

Strong reputation

The major pharmaceutical industries outsource their work largely on the basis of preferred partnership models and outsource to CROs based on their strong reputation and track records in handling diverse projects.^[19] According to the Center for the Study of Drug Development by Tufts University, top giant CROs including IQVIA, Syneos Health, Covance, Parexel, Wuxi AppTec, PPD, Charles River Labs, PRA Health Sciences, and Medpace dominate the maximum market share (approximately 57%).^[15]

Technical competency

Technical competency is measured by the capability and experience of CROs in conducting various projects in well-defined timelines. Past involvement of the CRO in conducting similar projects lowers the risk of failures.

Global outreach and understanding of regulatory framework

Quality control and assurance are the two main determinants for regulatory filing. International CROs open various global offices in different locations to access skilled professionals with knowledge of local drug regulatory process. The CROs conduct Phase 3 trials required by the national regulatory agencies to approve and market the drug in that region. In countries like India, one of the largest generic drug producers, sponsors approach CROs to conduct bioequivalence and biosimilar studies to gain access to generic drug manufacturing. Hence, knowledge of national regulatory framework becomes essential for the CROs to complete various tasks.

Expertise in defined therapeutic domain

Therapeutic expertise in the defined domain is important for clinical excellence. CROs with "ace team" of expert scientists and managers can efficiently complete the

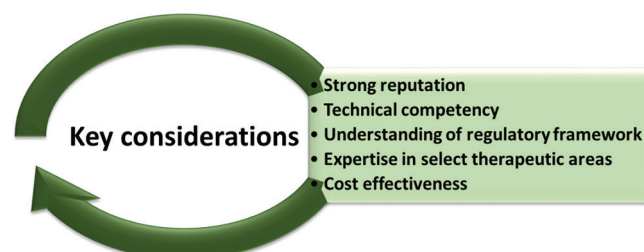


Figure 2: Key considerations in selecting a contract research organization

targeted task with high-quality data generation within a stipulated time. Therefore, it is important to partner with an experienced CRO having sound understanding of drug development process and wide therapeutic area expertise.

Cost-effectiveness

Cost is an important determinant in selecting a CRO, but it comes at a lower rank in overall selection process as commoditizing at a lower contract price can be a quality killer. It takes additional cost and time to handle the failed experiment.

Benefits and Challenges of Outsourcing

Benefits

Cost reduction

Decreasing profits have become a major concern for the pharmaceutical industry. Above this, the patent cliff has brought additional strain in the pharma-biotech world. Reports from Evaluate Pharma revealed a risk of 252 billion USD loss due to patent expiration of many drugs in the period between 2020 and 2026.^[29] Rising cost of R&D, decline in innovative potential, and approaching patent expirations are forcing companies to develop new strategies to increase their revenues. In most cases, it becomes cheaper to outsource some or all the R&D activities to designated CROs than to create and maintain in-house facilities.

Rapid drug discovery and development

Exponentially growing diseases and health needs require rapid drug discovery and development, which can improve with interdisciplinary approach. Outsourcing through different models at various stages of drug development will decrease the cost as well as increase the speed, as specialized and diversified CROs already have trained research personnel in different domains to carry out designated tasks.

Chasing innovations

Stochastic nature of drug development involving a huge investment risk has forced the companies to reduce in-house R&D, leading to decline in innovation. To uplift their weakened internal innovative potential, sponsors tend to outsource or partner with academic institutions for the initial drug discovery phase and then with private CROs, for translation into a potential new therapy in the later stages of drug development and commercialization. The development of Evusheld (AZD7442; tixagevimab/cilgavimab monoclonal antibody combination) is an example of such collaboration between academia, industry, and private CROs. Initial preclinical experiments at Vanderbilt University Medical Center showed that a combination of two potent monoclonal antibodies synergistically neutralized SARS-CoV-2 virus. In June 2020, it was licensed to AstraZeneca, who further optimized its half-life and reduced Fc receptor binding.^[30] Later, AstraZeneca successfully conducted clinical trials for Evusheld in collaboration with IQVIA and was later granted FDA emergency use authorization in December 2021.^[31]

Accessing therapeutic expertise and technologies

In the last decades, CROs have equipped themselves with advanced technical expertise along with efficient scientific workforce. Hence, sponsors prefer to outsource the drug discovery program to specialized CROs which provide them advanced state-of-the-art facilities. For example, Thermo Fisher Scientific, a leading biotechnology company, provides outsourcing services for therapeutics and vaccine development to various pharmaceutical companies.^[32] Figure 3 represents benefits of outsourcing to the CROs.

Challenges

Management challenges

Biopharmaceutical industry faces a major challenge in selecting, monitoring, and managing the services

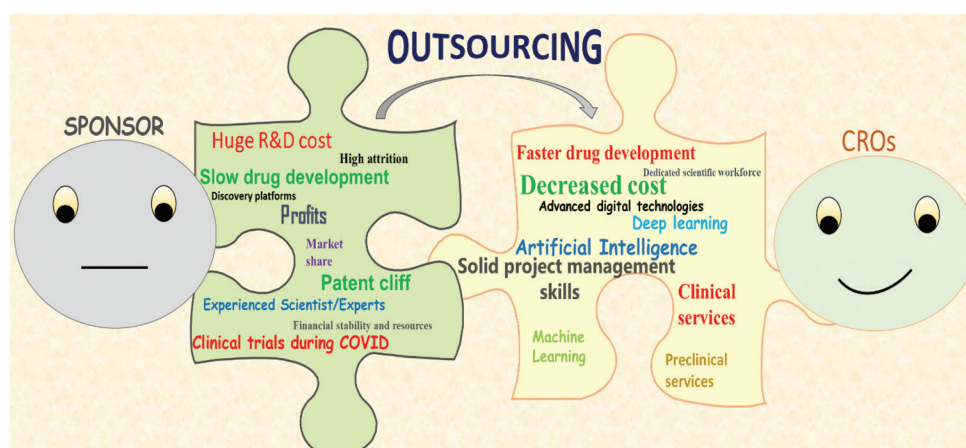


Figure 3: Processes being outsourced from CROs. CROs = Contract research organization

provided by CROs. Sometimes, the cost of managing an outsourcing operation gets more than having an in-house facility. CROs with good relationship, in terms of communication, compliance, and capacity, build trust over time and make the operations smoother. The overall goal in outsourcing services should be to develop mutually productive and predictive relationship. CROs should have the capacity to deal with individual project challenges and uncertainties. They should have a good data archiving system so that if a sponsor or regulator requires re-examination of all previous data, the CRO should be able to respond appropriately and quickly. There should be quality assurance in terms of compliance with regulations and guidelines. Managing such factors is a challenging task for sponsors.

Loss of cumulative knowledge base

Due to outsourcing, the in-house R&D capability of sponsors as well as “learning by doing” process gets weakened. The complete knowledge of drug’s life cycle, from birth to clinic, gets dizzy. CRO scientists must finish the assigned task without getting too curious about its further development as the next step may be handled by some other outsourcing team. Even if they find a molecule with certain outstanding properties, they must stop their inquisitiveness following confidentiality agreement and must move on to the next. This fades the charm of doing science. A decline in-house knowledge and expertise may be responsible for the increased M&A, as pharmaceutical companies need to maintain continual scientific rigor for drug development.

Operational stability and reliability of contract research organization

It is important to understand the operational stability of CROs and certainty that it will not go out of business during the study period. The major risk in outsourcing clinical trials is the failure of CROs in producing clinical data of acceptable quality to the regulatory agencies. The rejection of trial report by the FDA or any regulatory agency can pose an enormous financial burden as well as loss of time for sponsor and additional work for CRO. This can also delay product launch to the market causing huge revenue loss. The over-promise and under-delivery of outsourcing services by CROs can be troublesome for the sponsors.

Impact of COVID-19 on Outsourcing

The COVID-19 pandemic had severely affected the traditional way of conducting clinical trials. Unprecedented restrictions made clinical trial operations difficult leading to either suspensions or premature stoppage. Approximately, 80% of non-COVID clinical

trial-related activities were disrupted.^[33] As an effective readjustment to disrupted trial activities, swift adoption of computational technology-based virtual trials (a type of decentralized trial) gained momentum during COVID-19 pandemic.^[34] Decentralized clinical trials also known as a site-less, hybrid remote or virtual clinical trials, which focusses on patient-centricity rather than site-centricity, give patients considerably more flexibility in the way they participate.^[35] Decentralized approaches often rely on technology, such as mobile phone applications and smartwatches, to engage with patients (virtual trials), but may also utilize more dispersed local clinics or home health providers to “decentralize” some, or all data collected in a trial (hybrid trials).^[36,37] Although the idea of decentralized trial dates back to early 2000, the first virtual clinical trial, a pilot study, was conducted by Pfizer in 2011 to assess the validity of this new approach.^[38] In virtual decentralized trial, all the trial activities ranging from patient recruitment, drug dispensing, and data acquisition occur without in-person contact between the clinical trial investigating team and patients.^[39] Quick adoption of virtual tools such as telemedicine, real-time video conferencing, smartphone health applications, health monitoring devices, and patient-driven virtual health-care interfaces has made it possible to reach directly to patients at their home. The first fully virtual in-house, randomized, double-blind, placebo-controlled trial was conducted by Feinstein Institutes for Medical Research and Cold Spring Harbor Laboratory to evaluate the safety and efficacy of famotidine in mild-moderate COVID-19 patients.^[40]

Interestingly, shortly before the pandemic, the Heartline trial (NCT04276441), a virtual (the first-of-its-kind) study was launched in February 2020, by Johnson and Johnson to explore if a new iPhone app and Apple watch can decrease the risk of stroke by identifying and diagnosing atrial fibrillation at an early stage. Thanks to the virtual trial model, the recruitment was possible even during pandemic and is still recruiting.^[41]

Several CROs and eClinical software providers (IQVIA, Parexel, ICON, Science 37, Medable, Covance, PRA, ERT, etc.) have expanded their domains in the area of virtual clinical trials.^[42] This is evident by an exponential increase in strategic partnerships (57 deals in 2020–2021 in comparison to 19 deals in 2018–2019) and M&A deals (15 deals in 2020–2021 in comparison to 5 in 2018–2019). Some examples of the expansions of virtual trial space include ICON’s acquisition of PRA Health Sciences, ERT’s acquisition of wearable device-making company APDM followed by merging with Bioclinica, leading to emerging expertise in attaining technology-based clinical trial endpoints.^[43] In recent times, the use of IQVIA’s virtual trial solution platform in more than 60 trials by various big pharma companies such as Johnson and

Johnson and AstraZeneca is another example of virtual trial's vertical growth. Many of these virtual trials were launched in 2020 during the global pandemic.^[44]

Recruiting patients and collecting information by decentralized trials have gradually improved the patients' and physicians' experience. Initially, there were a lot of key concerns over data reliability and quality; however, by December 2020, 72% of the investigator physicians reported similar or even better experience with these decentralized trials in comparison to in-person visits.^[45] To overcome the concerns over data integrity in decentralized clinical trials, FDA is looking forward to "Cures 2.0 Act" to offer guidance on regulation of decentralized clinical trials.^[46] The proposed bill contains provisions to accelerate medical research, increase patient access to novel therapeutics, and remove current barriers to telehealth services.^[47]

Further, computational techniques such as AI and ML have swiftly woven themselves in clinical trial framework during COVID-19 pandemic for drug discovery and repurposing, generating 6 billion USD in the year 2020.^[48] Various vaccines including mRNA vaccines were developed within a year, which was an astonishing achievement and a work of collaboration. As the new variants are continuously emerging, there will be a need of other therapeutic agents (peptides, antibodies, small molecules, etc.) including vaccines in future. This can be possible in short frame of time with the use of quick virtual screening by learning-prediction model of AI, ML, and deep learning platforms. Beck *et al.*^[49] computationally identified the inhibitory potency of several known antiviral drugs such as ritonavir, atazanavir, and remdesivir against SARS-CoV-2 infections using the Molecule Transformer-Drug Target Interaction (DTI) model, a deep learning-based DTI prediction model. Similarly, Eli Lilly's drug Olumiant (baricitinib) was identified by ML and AI startup, BenevolentAI, for its potential to treat COVID-19 and went on to receive emergency use authorization by the US FDA in November 2020.^[50] Benevolent AI's ML and AI experts took just 3 days to identify six approved drugs showing promising efficacy against COVID-19. In a similar way, Repurpose.AI collaborated with Scripps Research by leveraging its ActivPred AI Drug Discovery Platform for the identification of potential drug candidates for COVID-19.^[27]

The extent to which virtual tools, AI, and ML platforms were adopted during COVID-19 are commendable. The emerging use of these evolving technologies in R&D is going to stay for long. It is important to maintain appropriate ecosystem for drug development through public-private partnerships, outsourcing models, and M&A strategies, so that the strength and expertise of

all can be utilized together as the prediction of another pandemic in the next decades cannot be ruled out.

Conclusion

Post-COVID scenarios have shown that CROs will continue to expand by adopting and providing innovative technologies including use of AI, ML, and virtual trials to bring the drugs or devices from the concept stage to the market, faster than ever. Future trends also suggest that drug or device companies with limited financial resources, high cost of maintaining R&D facility, and approaching patent cliffs will prefer to go for strategies like M&A and getting their drug developmental services outsourced from technically competent CROs.

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Conflicts of interest

There are no conflicts of interest.

References

1. Wouters OJ, McKee M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. *JAMA* 2020;323:844-53.
2. The Benefits of Outsourcing R&D Processes to CROs; 2021. Available from: <https://www.bioagilityix.com/blog/2021/02/02/the-benefits-of-outsourcing-rd-processes-to-cros/>. [Last accessed on 2022 Jan 13].
3. Simoens S, Huys I. R&D costs of new medicines: A landscape analysis. *Front Med (Lausanne)* 2021;8:760762.
4. Squires DJ. Outsourcing Drug Development; 2002. Available from: <https://www.contractpharma.com/issues/2002-10/view-features/outsourcing-drug-development/>. [Last accessed on 2022 Jan 09].
5. Buvaio A. The Evolving Pharma R&D Outsourcing Industry: A Bird's Eye View; 2020. Available from: <https://www.biopharmatrend.com/post/146-the-evolving-pharma-rd-outsourcing-industry-a-birds-eye-view/>. [Last accessed on 2022 Jan 14].
6. Contract Research Organization (CRO) Services Market Size, Share and Industry Analysis by Service Type (Discovery, Preclinical, Clinical, Laboratory Services), by Application (Oncology, Cardiology, Infectious Disease, Metabolic Disorders, Others) by End User (Pharmaceutical & Biotechnological Companies, Medical Device Companies, Academic & Research Institutes, Others), and Regional Forecast; 2019-2016; 2019. Available from: <https://www.fortunebusinessinsights.com/industry-reports/contract-research-organization-cro-services-market-100864/>. [Last accessed on 2022 Jan 17].
7. Demand for Global Contract Research Organization Market; 2022. Available from: <https://www.globenewswire.com/en/news-release/2022/07/14/2479973/0/en/Demand-for-Global-Contract-Research-Organization-Market-Size-Share-to-Surpass-USD-65-5-Billion-by-2028-Exhibit-a-CAGR-of-6-4-CRO-Industry-Trends-Value-Analysis-Forecast-Report-by-F.html>. [Last accessed on 2022 Aug 31].
8. India CRO Market Size, Share, Growth & Forecast 2027 | BlueWeave; 2021. Available from: <https://www.blueweaveconsulting.com/report/india-cro-market-information-bwc2070/>. [Last accessed on 2022 Jan 17].

- on 2022 Jan 14].
9. Fact Sheet On Foreign Direct Investment (FDI 2021); 2021. Available from: <https://dpiit.gov.in/sites/default/files/FDI-Factsheet-March%2C21.pdf>. [Last accessed on 2022 Jan 22].
 10. Vaidyanathan G. India's clinical-trial rules to speed up drug approvals. *Nature* 2019. [Doi: 10.1038/D41586-019-01054-4].
 11. Gupta YK, Padhy BM. India's growing participation in global clinical trials. *Trends Pharmacol Sci* 2011;32:327-9.
 12. Sacks LV, Shamsuddin HH, Yasinskaya YI, Bouri K, Lanthier ML, Sherman RE. Scientific and regulatory reasons for delay and denial of FDA approval of initial applications for new drugs, 2000-2012. *JAMA* 2014;311:378-84.
 13. IQVIA and AstraZeneca Team-Up to Support Development of Potential COVID-19 Vaccine – IQVIA. Available from: <https://www.iqvia.com/newsroom/2020/07/iqvia-and-astrazeneca-team-up-to-support-development-of-potential-covid-19-vaccine>. [Last accessed on 2022 Jan 27].
 14. Covance and Novartis Institutes for Biomedical Research. Available from: https://slidelegend.com/covance-and-novartis-institutes-for-biomedical-research-nibr_59dc38aa1723dd6ec7b22193.html. [Last accessed on 2021 Dec 27].
 15. Spinner J. Parexel, Pfizer Extend drug Development Partnership; 2020. Available from: <https://www.outsourcing-pharma.com/Article/2020/09/22/Parexel-Pfizer-extend-drug-development-partnership/>. [Last accessed on 2022 Jan 12].
 16. Top 5 Corporate-Academic Collaborations in Biomedical Sciences | News | Nature Index; 2019. Available from: <https://www.natureindex.com/news-blog/top-corporate-academic-collaborations-biomedical-sciences/>. [Last accessed on 2022 Jan 21].
 17. Steadman VA. Drug discovery: Collaborations between contract research organizations and the pharmaceutical industry. *ACS Med Chem Lett* 2018;9:581-3.
 18. Talley-Roithner E, King T. Strategically Selecting the Right Outsourcing Model for Drug Development – Considerations for Emerging Biotech; 2020. Available from: <https://www.ppd.com/blog/strategically-selecting-the-right-outsourcing-model-for-drug-development/>. [Last accessed on 2022 Jan 14].
 19. Sariola S, Ravindran D, Kumar A, Jeffery R. Big-pharmaceuticalisation: Clinical trials and contract research organisations in India. *Soc Sci Med* 2015;131:239-46.
 20. What Drives Pharma m&a? McKinsey. Available from: <https://www.mckinsey.com/business-functions/strategy-and-corporate-finance/our-insights/whats-behind-the-pharmaceutical-sectors-m-and-a-push>. [Last accessed on 2021 Dec 30].
 21. Understanding a Dynamic Industry Through Mergers and Acquisitions. Available from: <https://www.pharmasmanac.com/articles/understanding-a-dynamic-industry-through-mergers-and-acquisitions/>. [Last accessed on 2021 Dec 30].
 22. Keown A. M&A Will Continue to be a Mainstay for Growth in the Pharma Industry. *BioSpace*. Available from: <https://www.biospace.com/article/big-m-and-a-deals-will-likely-continue-a-nalyst-predicts/>. [Last accessed on 2021 Dec 30].
 23. Keown A. 2021's Top Biopharma Mergers and Acquisitions. *BioSpace*. Available from: <https://www.biospace.com/article/top-biopharma-m-and-a-activity-in-2021/?s=79>. [Last accessed on 2021 Dec 30].
 24. Taylor P. The Top 10 Biopharma M&A Deals in 2021. *Fierce Pharma*; 2022. Available from: <https://www.fiercepharma.com/special-report/top-10-biopharma-m-a-deals-2021>. [Last accessed on 2022 Aug 31].
 25. Sanofi Launches Dedicated Vaccines mRNA Center of Excellence. Press Release. Available from: <https://www.sanofi.com/en/media-room/press-releases/2021-06-29-08-00-40-2254458>. [Last accessed on 2022 Sep 01].
 26. Parrish M. What's Behind all the M&A Deals in Pharma? Available from: <https://www.pharmamanufacturing.com/articles/2019/whats-behind-all-the-m-and-a-deals-in-pharma>. [Last accessed on 2021 Dec 30].
 27. Big Pharma Forging More Partnerships with AI Vendors for Drug Discovery. Available from: <https://www.clinicaltrialsarena.com/comment/big-pharma-ai-partnerships>. [Last accessed on 2022 Jan 07].
 28. Shih MS. Roles of contract research organizations in translational medicine. *J Orthop Transl* 2015;3:85-8.
 29. Evaluate Pharma World Preview 2020, Outlook to 2026. Evaluate. Available from: <https://www.evaluate.com/thought-leadership/pharma/evaluatepharma-world-preview-2020-outlook-2026>. [Last accessed on 2022 Sep 01].
 30. COVID-19 Long-Acting AntiBody (LAAB) Combination AZD7442 Rapidly Advances Into Phase III Clinical Trials. Available from: <https://www.astrazeneca.com/media-centre/press-releases/2020/covid-19-long-acting-antibody-laab-combination-azd7442-rapidly-advances-into-phase-iii-clinical-trials.html>. [Last accessed on 2022 Jan 10].
 31. Coronavirus (COVID-19) Update: FDA Authorizes New Long-Acting Monoclonal Antibodies for Pre-Exposure Prevention of COVID-19 in Certain Individuals | FDA. Available from: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure>. [Last accessed on 2022 Jan 10].
 32. Biotechnology Commercialization, Thermo Fisher Scientific. Available from: <https://www.thermofisher.com/in/en/home/biotech-lab-solutions.html#menu1>. [Last accessed on 2022 Jan 04].
 33. Stepping Up the Decentralization of Clinical Trials. McKinsey. Available from: <https://www.mckinsey.com/industries/life-sciences/our-insights/no-place-like-home-stepping-up-the-decentralization-of-clinical-trials>. [Last accessed on 2022 Jan 07].
 34. van Dorn A. COVID-19 and readjusting clinical trials. *Lancet* 2020;396:523-4.
 35. de Las Heras B, Daehnke A, Saini KS, Harris M, Morrison K, Aguilo A, *et al.* Role of decentralized clinical trials in cancer drug development: Results from a survey of oncologists and patients. *Digit Health* 2022;8:20552076221099997.
 36. Goodson N, Wicks P, Morgan J, Hashem L, Callinan S, Reites J. Opportunities and counterintuitive challenges for decentralized clinical trials to broaden participant inclusion. *NPJ Digit Med* 2022;5:58.
 37. Decentralized, Virtual, or Hybrid Clinical Trial – What's the Difference? – ArcheMedX. Available from: <https://www.archemedx.com/corp-blog/decentralized-virtual-hybrid-clinical-trial-whats-the-difference>. [Last accessed on 2022 Aug 31].
 38. Pfizer Conducts First "Virtual" Clinical Trial Allowing Patients to Participate Regardless of Geography, Pfizer. Available from: <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-conducts-first-virtual-clinical-trial-allowing-patients-to-participate-regardless-of-geography>. [Last accessed on 2022 Jan 11].
 39. Van Norman GA. Decentralized clinical trials: The future of medical product development? *JACC Basic Transl Sci* 2021;6:384-7.
 40. Brennan CM, Nadella S, Zhao X, Dima RJ, Jordan-Martin N, Demestichas BR, *et al.* Oral famotidine versus placebo in non-hospitalised patients with COVID-19: A randomised, double-blind, data-intense, phase 2 clinical trial. *Gut* 2022;71:879-88.
 41. A Study to Investigate if Early Atrial Fibrillation (AF) Diagnosis Reduces Risk of Events Like Stroke in the Real World. Available from: <https://clinicaltrials.gov/ct2/show/NCT04276441>. [Last accessed on 2022 Sep 01].
 42. Katsarova N. 17 Virtual Clinical Trial Providers to Partner Up With, TrialHub Available from: <https://trialhub.findmecure.com/blog/articles/virtual-clinical-trial-providers/>. [Last

- accessed on 2022 Jan 07].
43. Significant Increase in Virtual Trial Deals Since 2020 as a Result of COVID-19. Available from: <https://www.pharmaceutical-technology.com/comment/significant-increase-virtual-trial-2020-covid-19>. [Last accessed on 2022 Jan 07].
 44. IQVIA Holdings Inc – IQVIA Virtual Trial Solutions Used in More than 60 Trials. Available from: <https://ir.iqvia.com/press-releases/press-release-details/2021/IQVIA-Virtual-Trial-Solutions-Used-in-More-than-60-Trials/default.aspx>. [Last accessed on 2022 Jan 07].
 45. Fact Sheet IQVIA Decentralized Trials. IQVIA. Available from: <https://www.iqvia.com/-/media/iqvia/pdfs/library/fact-sheets/iqvia-virtual-trials.pdf>. [Last accessed on 2022 Sep 01].
 46. Banks MA. Core concept: In the wake of COVID-19, decentralized clinical trials move to center stage. *Proc Natl Acad Sci U S A* 2021;118:e2119097118.
 47. Patel D, Rosen DL, Walsh JF, Rifis JB. The Proposed Cure 2.0 Act—What You Can Expect. Available from: <https://www.natlawreview.com/article/proposed-cures-20-act-what-you-can-expect>. [Last accessed on 2022 Jan 11].
 48. The Future of Clinical Trials: The Promise of AI and the Role of Big Tech; 2021. Available from: <https://www.cbinsights.com/research/clinical-trials-ai-tech-disruption>. [Last accessed on 2022 Jan 11].
 49. Beck BR, Shin B, Choi Y, Park S, Kang K. Predicting commercially available antiviral drugs that may act on the novel coronavirus (SARS-CoV-2) through a drug-target interaction deep learning model. *Comput Struct Biotechnol J* 2020;18:784-90.
 50. Richardson PJ, Corbellino M, Stebbing J. Baricitinib for COVID-19: A suitable treatment? – Authors' reply. *Lancet Infect Dis* 2020;20:1013-4.