Blockchain for increased trust in observational studies

A blockchain is a decentralised database allowing different stakeholders to obtain local copies of data and to be involved in how each data item is integrated into the database. Stakeholders can manipulate data in a privacy-preserving environment and the database should be immutable. Within this environment, data are time-stamped and added sequentially (by block), thus potentially guaranteeing their traceability and chronology (time-ordering). Furthermore, executable code that runs on top of the blockchain (called a smart contract) enables automation of some routine processes and allows comparison of timestamps that constitutes time-ordering.

Blockchain technology could enable the consolidation of data traceability in clinical research and might have enabled earlier discovery of the scientific misconduct related to the COVID-19 hydroxychloroquine controversy.[1,2] In Mehra and colleagues' retracted study[1] in *The Lancet*, the authors analysed data from 96 000 reports of patients with COVID-19, allegedly collected from an international network of hospitals and provided by the company Surgisphere. Readers observed disparities between the study data and data from the Johns Hopkins University clinical database. Most of the authors (except the author associated with Surgisphere) and the reviewers did not have reliable means of verifying the quality or authenticity of the primary data. Blockchain could have been used to trace the data from original collection through to analysis.[3] Blockchain could also have enabled a secure environment for data sharing to consolidate and verify results.

At the same time, the study by Lagier and colleagues[2] that has been widely commented upon,[4] which compared hydroxychloroquine with standard of care in patients with COVID-19 and claimed to have shown hydroxychloroquine's superiority, also raised numerous issues. For example, the intention-to-treat principle was not observed and patients who received hydroxychloroquine and whose condition worsened were moved into the control group.[4] Blockchain can been used to track each participant's data, maintaining time-ordering of data between inclusion and follow-up. Application of a smart contract could also have resolved questions raised about patient consent in this study.

More generally, blockchain's ability to consistently track clinical study events and prevent after-the-fact protocol violations could make this technology a key adjuvant for observational studies. In a seminal paper, Feinstein[5] pointed out that many medical questions cannot be studied using randomised controlled trials (RCTs): both RCTs and observational studies are needed. Furthermore, some advantages of RCTs are unrelated to the randomisation process itself, but instead involve research planning (eg, the existence of a protocol and admission criteria). Ioannidis[6] underlined that observational studies can provide straightforward, low-cost clinical evidence, as long as essential information (the protocol, data collection, and analysis plan) can be registered. No equivalent of ClinicalTrials.gov exists for observational studies, unfortunately. This absence of a strong methodological guarantee for the evidence derived from these studies could impair trust in their reliability.

This is where blockchain could strengthen results from observational studies, by proving the protocol's existence, tracking its updates, confirming that the analysis plan preceded its execution, and tracing the data-sharing policy. Observational studies done with blockchain data recording would benefit by enhanced reliability of their results, leveraged potential for big data retrospective analysis through consolidating their designs and, in a pandemic context, quickly deployable designs with sharable, consistent results ensured.

We declare no competing interests.

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