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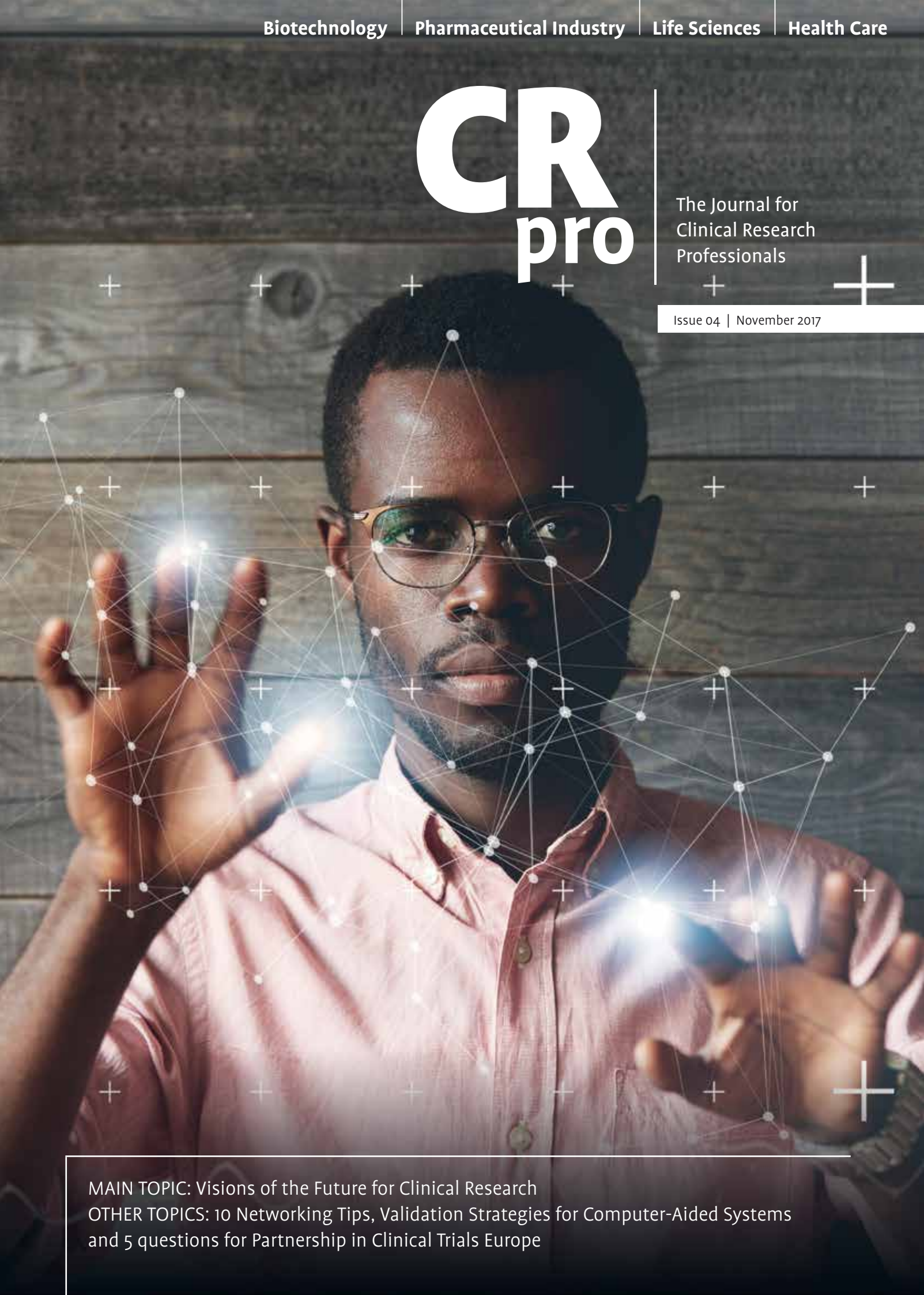

MAIN TOPIC: Visions of the Future for Clinical Research
OTHER TOPICS: 10 Networking Tips, Validation Strategies for Computer-Aided Systems and 5 questions for Partnership in Clinical Trials Europe

CR pro | Issue 04 | November 2017 | MAIN TOPIC: Artificial Intelligence and How It Changes Clinical Research?


MAIN TOPIC:

Visions of the Future for Clinical Research:

# *The Role of Artificial Intelligence and How It Changes Clinical Research*

*The synergy of advances in diverse areas of artificial intelligence holds considerable promise for improving the efficiency and efficacy of clinical trials. Our own focus is primarily on improving protocol design and execution, but there are many opportunities for improving the entire clinical trial process and each of these opportunities is of interest.*

The clinical trials process is costly, time-intensive, and replete with failures. As reported in [1], in the USA, only 32% of drugs survive Phase I and Phase II trials and go on to Phase III, and only 10% of potential drugs get approval. The cost of these failures is not known precisely, but are estimated at between $800 million and $1.4 billion per trial [2]. (The average cost per drug developed is at least $4 billion [3].) Phase III failures are due primarily to poor efficacy, unanticipated adverse events or serious adverse events, or a failure to demonstrate commercial viability. Drugs also fail to be approved because of insufficient information provided to regulatory agencies (such as the Food and Drug Administration). This is the case in an estimated 50% of new molecular entities applications. [4] Furthermore, low enrollment and retention rates lead to failed clinical trials; for example, 1 in 4 cancer trials fail to enroll sufficient patients [5]. Recruitment material may also fail to attract patients [6].

Of particular interest to our efforts is improving the design and execution of research protocols. Poorly constructed protocols lead to poor research, and potentially to numerous costly amendments, protocol deviations, delays in obtaining appropriate data, and other problems [7]. Protocol deviations are not rare, occurring in around 15.6% to 24.9% of all enrolled patients in studied Phase III trials [8,9]. Furthermore, failure to report protocol deviations is a current issue: In a recent study, 32% of included trials did not provide any explicit reports of any type of protocol deviation [10].

## How Artificial Intelligence Could Improve Outcomes

The artificial intelligence (AI) system we are building is designed to receive a protocol document, scan it, and assess it for various characteristics of interest. This includes, for example, the consistency between the time and events (T&E) table and the in-text description of events, and the consistency between the synopsis and the body of the protocol. Natural language processing tools can be helpful in this regard, but greater methods of knowledge extraction can provide real insights.

AI tools can be used to scan other published protocols based on a similarity measurement, which may include criteria such as the indication for treatment, primary and secondary objectives, whether the study involves pharmacokinetics and pharmacodynamics, safety objectives, whether the study involves a drug or a device, the type of study (e.g., randomized, blinded), and so forth. Similar protocols can then be coupled with published or internal data, indicating the degree of success from the experimental design as well as any problematic items. Concerns can then be flagged for the study designer for further consideration.

## Addressing Enrollment and Retention

Clinical trials sometimes fail because of poor enrollment rates. Having an AI system warn the study designer, for example, that particular inclusion/exclusion criteria may be too limiting for subject enrollment can save the sponsor considerable funds and time that can be invested in a better clinical design or an alternative effort. Clinical trials also fail at times because of poor subject retention. To address this, we have created and are refining what we describe as a Patient Burden Index (PBI), which is an AI-derived quantitative measurement of the impact that the protocol design has on the patient or subject. Our measurement includes factors such as the anticipated distance that subjects must travel to reach a study site, the time spent at the site and in the study, anticipated pain level and the duration of the pain level, average patient age, special considerations regarding known demographics of typical participants, and

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*Trials.ai is Kim's 3rd company yet her passion for fixing logistical problems with clinical trials drives her as if it were her first. Her expertise in organizational development enabled her build Corporate Development for companies like Pfizer, Merck and Wyeth Ayerst. Ms Walpole understands the complex clinical trials space and the needs of sponsors, CROs and sites. Her goal is to use technology to as a catalyst for helping organizations in study design and execution so that patients can be exposed to better quality treatments, faster*

other factors. Protocols can then be scored based on their PBI, and alternative designs can be compared with the patient in mind. We believe this is an entirely novel approach to improving subject retention and cooperation at all stages of a clinical trial.

### More Effective and Efficient Execution of the Trial

Once the trial has started, AI can play additional roles to help ensure the best outcome. In our case, our client partners provide a protocol that is uploaded into a system. The system then maps the T&E schedule into a dashboard-driven user interface that shows when each event shall be completed. With available personnel assignments and schedules, the system can also identify who shall do which task in support of which patient at which time. Practitioners are alerted ahead of time of windows for events, which helps to reduce protocol deviations. Any deviations from the protocol are noted and require an investigator or other approved person's acknowledgment and written explanation, if applicable.

### Patient Involvement and Focus

AI systems can also contact study participants, by email, phone, or text, to remind them of study events. This assists in maintaining study compliance, creating fewer protocol deviations and generating great subject retention. Throughout the study, the AI methods can provide an estimate of how likely the study will be completed, which can be helpful for the study coordinator to maintain cognizance over the trial.
AI can also assist practitioners in avoiding unnecessary medical issues for individual patients. Each patient's recorded medical and concomitant medications can be mined for indications of possible allergic reactions, drug interactions, or other issues. These can then be flagged for the study coordinator and principal investigator. This provides another opportunity to prevent misdosing or selecting an inappropriate medication to treat a treatment-emergent adverse event (AE), even if it may otherwise be the standard of care for the study site.

### AI for the Principal Investigator

AI can, in addition, help the principal investigator in determining plausibility of potential AEs resulting from a study drug or device. Fuzzy logic (i. e., computing with words) can be used to provide the practitioner with a linguistic description of plausibility rather than a purely quantitative response. With available subject information, the AI system can make treatment recommendations based on standard of care and individual subject needs, which could include insights for genomic data.

Any serious adverse events (SAEs) are noted in the system and require follow-up information regarding the circumstances, the degree of severity, treatment, possible relatedness, outcome, and any other information that the investigator believes is pertinent. The investigator can review these data in the form of a condensed narrative generated by the AI system and can better anticipate what a final narrative may look like.

As data are collected, the system aggregates data fields according to the statistical analysis plan (SAP) and allows data to be screened in different ways (e.g., providing a 2% cutoff table on adverse events by system, organ, class (SOC)). This function can be helpful in minimizing errors that may come later when transcribing data from tables and listings to a clinical study report (CSR).

### Visions for the Future of AI in Clinical Trials

The future of clinical research will involve AI at every stage, from initial drug discovery, study design and execution, to improved reporting and monitoring. Our focus is specifically on the clinical trial stage and leveraging various AI tools to help practitioners design more effective, less costly trials, with lower patient burden and greater patient retention. While AI is already being used for identifying opportunities for individualized treatment and computational drug design, we expect that AI will greatly facilitate future adaptive clinical trials and be a source of knowledge discovery for researchers and investigators in this crucially important area of application.

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*Dr. Fogel is chief science officer of Trials.ai. He has a 30+ year background in artificial intelligence and machine learning with numerous applications in medicine and biotechnology. Dr. Fogel has published over 200 papers in peer-reviewed literature and has received numerous awards from the IEEE and other professional organization. Dr. Fogel was the founding editor-in-chief of the IEEE Transactions on Evolutionary Computation and also served as editor-in-chief of BioSystems. He holds a Ph.D. from UCSD.*

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*Mike started his career as a Technology Strategy and Implementation consultant. His clients included some of the largest telecom companies in Europe, as well as the largest furniture retailer in the world. Mike has an MBA from the University of Rochester where he concentrated in Finance and Strategy. His passion for machine learning was crucial at Vergence Technologies where he lead operations and product strategy. Mike's diverse skill set, competitive attitude, and passion for teamwork are essential propellants to success at Trials.ai.*

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