Applying complexity theory to model the operation of clinical trials in human communities

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Abstract

Background When a vaccine clinical trial enters a human community two independent systems merge into one system with various levels if interdependence. This system exhibits non-linearity and unpredictability, creating challenges for the research team. In this study we explore the researcher experience during clinical trials in human communities, through the lens of complexity theory. Methods We conducted in-depth interviews with a total of 11 researchers working on a phase III vaccine clinical trial in Kenya (Registry name: RTS,S ClinicalTrials.gov; Registry number: NCT00866619; Registry date: March 20, 2009). The interviews captured the researcher's experience of working in a complex adaptive system and were analysed using thematic coding. Results Both human communities and clinical trials have the attributes characteristic of complex adaptive systems. Challenges researchers encountered working in this merged system include rumours, suspicion related to blood draws, and misconceptions. The researchers highlighted that a foundation of trust and open communication were foundational blocks to embrace the non-linearity of the system. Conclusions We have identified the key role that complexity theory plays in improving clinical trial design. The factors identified by our respondents, as seen through the lens of complexity theory, are integral to informing how clinical trial research can be tailored to the local social setting. Understanding the system (community and trial) as one allowed for the identification of patterns that influence the emergence of the system. This calls for clinical trial design to incorporate iterative practices to better equip research teams to adapt to the emerging behaviour of the system.

Background

Clinical trials are a critical part of the vaccine development process to establish both the safety and effectiveness of a vaccine. Vaccine clinical trials have extensive regulatory requirements and operational components to adhere to.(1) These clinical trials take place in human communities where elaborate social networks and environmental factors form the community. When research such as vaccine clinical trials enter into a community, a complex array of considerations come into play and affect the outcome of the research. Considerations specifically relevant to the social complexity of the community and the regulatory complexity of the clinical trial.

There are particular considerations specific to clinical trials being conducted in low-resource settings. The majority of vaccines currently in the development pipeline target diseases endemic to populations living in these settings.(2) These considerations are unique due to the large resource discrepancy, with a high-capital vaccine clinical trial centre conducting research in a low-capital clinical trial site within which the communities are located. This has significant implications for communication, benefit-sharing and engagement with the community.(3) To explore these implications, we take the unique approach of utilizing complexity theory to explore the unfolding of a new complex adaptive system (CAS) when a clinical trial conducts research in a community. (4–7)

Here we investigate the experience of two vaccine clinical trial research teams working in communities in Kenya. We have selected a phase III clinical trial of the leading malaria vaccine, RTS,S, to study the interplay of the research team with the community. This multinational, phase III study was carried out across seven countries/systems and cultures with rigorous, standardized regularity requirements in all eleven trial centres.(8) These regularity demands on research teams occur in vastly different contexts. With a focus on Kenya, we look

through the lens of the researchers working in the community during the phase III malaria vaccine clinical trial. In 2019, this vaccine will be rolled out in phase IV studies in three different African countries.(9) This vaccine clinical trial is therefore characteristic of large, multinational clinical trials operating in a low-resource setting. This clinical trial team has proven to effectively work with the community such that the research will continue into a phase IV study. Through this evaluation we shall better understand the factors at play when a complex clinical trial system enters a complex social system.

Complexity theory is a useful framework for vaccine clinical trials operating in low-resource settings. Communities and clinical trials are CAS.(4–7) The conduct of vaccine trials merge two CAS, the clinical trial and the community, into a new system. In essence, CAS describe systems that have components of non-linearity, iteration, unpredictability, interdependence and emergence.(10–12) Cilliers (1998) outlines a CAS as a system with a history that impacts the current state and its evolution, a system that has many concurrent interactions which are characterized by feedback loops and is open to the external environment.(13) Based on these attributes, the merging of a complex trial system and a complex social system requires prospective considerations for researchers working in vaccine development. To better understand these considerations and their consequences, the experience of researchers in this phase III malaria vaccine clinical trial in Kenya is evaluated. This understanding can strengthen clinical trial through prospective integration into clinical trial design.

Methods

In order to capture the researcher's experience in the community during a vaccine clinical trial in a low-resource setting, we conducted a series of in-depth qualitative interviews in March 2018 with members of the RTS,S phase III clinical trial. This study was part of a larger project looking at clinical trial research in low-resource settings and the methodology presented here relates to other work.(3)

Study Design

The phase III transnational clinical trial was carried out between March 2009 and January 2014 covering eleven clinical trial sites in seven African countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, United Republic of Tanzania). Upon the completion of the trial, post-trial epidemiological monitoring has continued to be done. All respondents were based in Kenya.

In-depth interviews

Interviewees were asked about their role as a researcher in the clinical trial, particularly their role in community engagement, focusing on relational dynamics and communication in relation to the formation of a CAS with the trial team and the community. Questions were also focused on identifying their personal perception of the community, both positive and negative, and the ways in which they responded to those experiences.

Purposive sampling was used, all respondents were researchers involved in the RTS,S malaria vaccine candidate phase III or post-study epidemiological monitoring (ClinicalTrials.gov Identifier NCT00866619). Trust was established by visiting the centre in March 2017 and introducing the study and its aims, maintaining regular contact and then returning to the clinical trial centre in March 2018 to conduct the interviews. The interviews were

conducted by the first author, MV, in English at the clinical trial centre. Interviews were conducted until saturation was reached.

Data analysis

Interviews were recorded, transcribed and then coded using MAXQDA software. Transcription began immediately after data collection and inductive detailed line-by-line microanalysis was utilized to identify categories in the data. Based on these categories, relationships were identified and organized into themes. All interviews were conducted, transcribed and analysed by the first author and parts of the coding were reviewed by the co-author SM. The focus of the analysis was on researcher values, lived experience and views on community engagement to best identify the CAS from the researcher's experience.

Ethics

Ethical approval was obtained from the Strathmore University IRB (SU-IRB) in Kenya and written informed consent was obtained from all respondents for the in-depth interviews. All data was anonymized by removing identifying factors and securely stored on a password protected computer.

Results

The results presented here relate to earlier work looking at the experience of caregivers of pediatric participants in malaria vaccine clinical trials.(3)

Eleven interviews were conducted with members of the research team. Respondents had various roles in the research team but all were involved with the RTS,S malaria vaccine clinical trial. The average length of an interview was 53 minutes, with the shortest being 28 minutes and the longest 2 hours.

In the interviews, respondents described their experience in the community and overall impressions with great detail. Respondents described communities as dynamic and outlined the experiences they had when working in community systems. In particular, challenges associated with blood draws, rumours and misconceptions arose, as well as the ways in which they dealt with these. Often a foundation of trust and continuous communication were reported to be key for clinical trials to work in a community and through complexity theory this foundation can be used to embrace the non-linearity of the system and effectively work in it. Below we present the alignment with these descriptions and CAS, as well as the indicators that when a clinical trial is initiated in a community they merge, and they exhibit interconnectedness and interdependence and behave as one cohesive system.

Communities are complex adaptive systems

The ways in which respondents defined community was strongly aligned with attributes related to unpredictability, non-linearity and emergence associated with complex adaptive systems. When discussing work in the communities, respondents described a dependency on a complex array of factors. Throughout the interviews, researchers brought up their definitions of community from their perspective, in particular the diversity across various communities and the ways in which this impacted the trial.

P11 Working with communities is dynamic. There are pros and cons about working with communities. But it depends on how you conduct yourself in the community and how you engage the community.

P10 It depends on the social make-up of the area where you are. For example, we had more withdrawals from the central area than from the more rural outlying clinics.

Challenges of working in CAS

The impact of misconceptions around adverse events and risks was reported by all respondents, which could vary depending on the community context. These misconceptions arose out of contextual factors within the community system, as there are multiple factors acting on the community simultaneously to the trial procedures. These also indicate the merging of two independent systems (trial and community) displaying significant interdependence. The challenge in dealing with this was also raised, particularly in sensitive cases when a participant has died from causes not related to the vaccine study. Here the community blames the powerful clinical trial for an event where helplessness is experienced in the community, indicative of a power imbalance and linked to the hierarchy characteristic of CAS. The non-linearity and complexity of working in CAS settings was evident, as well as the experience for the researcher being a part of the community system and then having to return to an unpredictable scenario.

P08: If for example after a participant dies, it becomes another challenge altogether because a participant can die from another cause. But then people sometimes feel that in a way you contributed to that. But you see those who are participating at least they know because they went through the whole treatment procedure and everything so then they understand. But now the whole community, even when you are going to visit these compounds you feel when you are going you are not really sure of what can take place, because you are going, and you don't know if maybe some people will turn wild and attack you or something. But then it never happened, really, actually, it never happened.

The interviews revealed consistently that there are many concerns from the community with regards to blood draws and transfusions, illustrating that communities are not operating in isolation, instead they are imbedded in contextual histories where clinical trials were, at times, exploitative. This overlapped with religious motives for denying medical intervention such as blood transfusion or oxygen for a sick child enrolled in the clinical trial. Many of the communities have rooted beliefs around blood, arising out of these historical research experiences.

P08: The main issue in the community is about blood samples that we take, that one is a major issue. People want to know "what are you doing with the blood?"

There are multiple factors that play into the consent process and it is rarely the person who consents (frequently the mother) who has the only say in the child's participation. The concerns around blood or other misconceptions are often heightened in those family or community members who haven't gone through the formal consent process. Different communities have varying employment realities, which contributes to the social make-up and transience of fathers at a given moment in time. This is not predictable and adds a layer of complexity to operating in a community.

P02: Some homes you had the father, or the head of the household, who does not want anything to do with vaccine research because of the perspectives. So they would be hostile. And threatened, "leave my home, I don't want my

children in those studies, you're taking blood for what? You're making money with our blood!"

In a few cases it was highlighted that external research projects being conducted in the area interfered with the perception of the research study. In particular, it was noted how some researchers bypassed community engagement processes. As the community did not necessary distinguish between research institutions due to the overlap of activities, this generated further broad suspicion around medical research.

P11: University students that don't know how to do it and they're in a hurry to get their data. They just say, take these 200 shillings, I want to remove the blood of the child. And the community kept on thinking it was us.

It was widely reported that having local staff was necessary for effective community engagement and necessary for an understanding by the trial team of the sociocultural norms and economic contexts unique to the participants. However, it was also acknowledged that in the event of an employment termination there could be a disruptive impact on the community-trial relationship. These explicit demands by the community for more reciprocity from the clinical trial was indicative of the community's experience with the power imbalance. The economic and power inequity was seen as a particularly delicate issue for the research team, in line with the hierarchal nature of CAS.

P02: There are instances where the family would say "My daughter was looking for a job but you never hire people here from this community, you want to bring people from outside to come and work for you" so probably a percentage of your field team should come from the community, because now the community relates, they know these people, these people live amongst them, there is no way they can bring something bad to them.

P02: We have a family around the community, one of their children was hired here but because of negligence, he used to miss, he lost his job. So the family was mad at the organization so they would go around the community and discourage people from engaging with us.

How researchers work in complex adaptive systems

It was cross-cutting across respondents how important it was to understand the people in the community, show concern and express gratitude for their participation. This was an important aspect to working harmoniously in the community through strengthening the communication and comprehension. At times, the researchers identified the power imbalance within the CAS between the clinical trial and the community, feeling that more needed to be done for the community and the participants.

P02: Think about their needs and don't treat them as a subject, treat them as someone who has sacrificed their time who has put aside some of the things they were supposed to do to come to the clinic.

P07: You get to learn their challenges, or their fears, or their reservations. And then you get to explain why you are doing what you are doing at that time point and why you are planning to do it or why you are not planning to do it.

Understanding the role of community leaders, especially elected leaders, attributed to positive opinion of the trial within the community – as they can have a major impact in the community and determine the directionality of the engagement. It requires careful engagement by the research team, as it is necessary for the success of the trial to have the chief's support.

P05: And the chiefs, those ones you must have on your side, before you try anything. Because if they decide you treated them disrespectfully that study is not going onwards, they'll say don't enroll, they're doing this, maybe they're selling blood.

Being aware of the norms and subsequently approaching misperceptions in accordance with those norms was reported as being a continual iterative learning process. For instance, addressing power dimensions and sending the appropriate staff member to provide clarification in challenging situations. A few respondents clearly identified how important it is to have members of research team that are culturally versed and sensitive to local norms. Without this there can be implications on perception of the study, without the researcher themselves being aware of it.

P05: He is familiar what not to do. Maybe when you enter a household, how you should enter, who you must see before you start seeing. You can't just enter a homestead and just start talking to anyone you want, it's inappropriate.

Frequently it was reported that staff should not only be properly trained, but also selected based on their fit within the community norms. This was seen as key to maintaining a trusting and strong relationship with community members.

P11: You must know who your staff are. Others are outgoing, others are introverts. You can't send an introvert to the village, they will be closed. The villagers will not share with them.

Respondents often brought up the role that trust plays in communicating with the community and maintaining harmony. The ways in which this was built was through consistent and transparent communication, as well as adhering to the proposed study protocol without surprising the community with new procedures.

P09: Trust is in the core of the understanding between the staff and the community.

Hosting information sessions that are inclusive to all members of the community (not only those who consent and the participants) was reported to be a positive contribution to the trial perception and addressing information gaps. It is helpful to have regular sessions where all can attend and have access to information updates to avoid a powerful voice having a misconception or information gap.

P11: Communicate and talk to them at every level. Right from the time they come to the clinic. To not be tired of communicating, communicate all the time.

Informing the community about research findings was also highlighted by the respondents. Especially in the long-term view of the research study and supporting future recruitment was identified to be tied closely to ongoing engagement and keeping the community informed.

P01: I think people want to know where you have reached, because especially if it is not a perfect vaccine, for the lack of another word, then people will need to come back again, provided that the disease remains a problem, to come back again to the community. That's a major challenge, especially for large studies.

The introduction of a new research project, in this case a new vaccine, required a lot of clarification and engagement. Especially ongoing involvement of the community to raise understanding and comfort with the new tool. The nature of this involvement was dependent on the community the research team was working in.

P08: What I have learned in this community, is that if there is a vaccine that is injected, a lot of mobilization needs to be done. Because you find that in these areas there are not many vaccine trials that previously had been done so people don't really know how the vaccine trial is done, especially one that is injected.

The establishment of the Community Advisory Board (CAB) was reported to be beneficial as a tool for staying aware of the community developments. Having regular meetings allowed the clinical trial team to address misconceptions and information gaps, as well as adapt appropriately to new situations.

P01: I would not start a study without telling the CAB, it would almost be suicide. If something goes wrong, even if you don't know who to tell, you see then you have already told them "oh remember the study, we discussed, oh this is what is happening" or they already know about it, so if they hear a rumour they can tell the people, we heard, but that is not really it.

A number of respondents identified the need to translate informed consent forms into contextually-sensitive language. It was reported that certain words translate poorly into the local language, with the consequence of creating community suspicion towards the researchers.

P04: Allowing the use of more latitude with how we translate, meaning it should not be word-for-word, which is what they tend to look at, but it should be more context.

Despite the various ways in which challenges were addressed and the overall benefits attributed to the clinical trial working in the community, a few respondents called for more to be done. These researchers felt that with the power of the clinical trial and the benefits received, the community needed to benefit more and the trial needed to do more in return and acknowledge this power discrepancy.

P02: Being an organization working in a community, you should give back to that community. You should show concern, don't just collect data and forget about them.

P07: Different communities have different expectations, it is really challenging because when we are starting the trial the new satellite facilities were looking forward to us doing much facility improvement.

Discussion

Clinical trials carried out in and merging with communities exhibit many attributes of complex adaptive systems including historical influence, dynamic interactions, nonlinearity and interdependency.(13,14) A useful definition by Neely (2015) describes a complex adaptive system as *a system in which agents are interconnected and interdependent and their individual actions form patterns of repetition that create emergent structures which have a non-linear influence on agent behaviour and further emergence*.(4) Drawing on this definition, the initial state includes an independent community system and an independent trial system, each governed by an independent

set of rules. Upon the initiation of the clinical trial in the research site, these systems merge and their components exhibit interconnectedness and interdependence. This leads to the generation of an entirely new CAS with a non-linear influence on system behaviour and emergence, open to the external environment. Through approaching clinical trial conduct in low-resource settings with the utilization of CAS, additional insight is provided through enabling the design to view the system holistically and equip researchers with tools that enables them to embrace the non-linearity and adapt effectively. Specifically, understanding clinical trials in this way allows for the identification of patterns that influence the emergence of the system and subsequently ways to address traditional components of research considered outside of research team control.

The community system has social networks, trial information sessions, family dynamics, employment, rumours, and a health system that lead to continual evolution of the CAS.(3) The trial system is operating within its own set of rules guided by sponsors, eligibility criteria, trial protocols, participants, Good Clinical Practice (GCP) guidelines, and payment terms. These two systems are also open, and thereby constantly in exchange with the external physical environment that carries with it influences from media, scientific progress, research studies, disease, ethics committees, and routine vaccination programs (figure 1). Between the community and trial, a significant power discrepancy is present, indicating which actors have a greater influence on CAS emergence. Each of these aspects was touched upon during the interviews and support CAS theory as a useful model for vaccine clinical trial research in low-resource settings. Therefore, approaching community relations during clinical trials in low-resource settings with implicit linear and mechanistic assumptions will see inconsistent outcomes. In contrast, we have found that clinical trials within communities is a deeply iterative process, dependent on feedback loops and the interaction of dynamic networks.

In this study the phase III malaria vaccine clinical trial was used as a case study to understand the consequences of two CAS merging and the prospective considerations of relevance for research teams working within this newly merged CAS. Figure 1 models the identified actors and the factors at play in shaping the behaviour of the system. Currently, clinical trials are designed with the assumption that the clinical trial system and the community system operate in isolation. However, the findings of our case study indicate that the emerging behaviour of the system contradicts this assumption. Therefore, denying the interconnectedness of the community and trial is detrimental to the success of the trial as it does not allow teams to adapt to unpredictable system behaviour. We found that challenges concerning rumours, community scepticism of a new vaccine, employing community members, minor events with unforeseen consequences and hierarchal structures are all behavioural indicators of one interconnected CAS. This CAS operatives with cyclical iterative feedback loops (figure 1) and requires researchers to respond in a similar iterative manner to these challenges. For the research team in this case study, a certain amount of iteration occurred informally and was needed for the trial to proceed in response to these challenges. Below we describe the emerging behavior of the system upon the merging of a clinical trial with a community. In particular the challenges identified by the researchers when carrying out a transnational clinical trial, adhering to standardized clinical trial regulations, while attempting to adapt to the non-linearity of the new system.

One of the main challenges reported by researchers is the difficulty in addressing misconceptions and preventing the spread of rumours, a concern frequently described in clinical trial research.(15,16) Our respondents identified

community concerns that highlighted commonly reported suspicions around blood, infertility and death in relation to the clinical trial.(15–19) As this is commonly reported during clinical trial research in low-resource settings, it is worthy of greater attention during clinical trial design.(3) Contextual and historical realities influence these rumours and simply providing access to the correct information alone is not sufficient to eliminate them - as they are shaped by the history of community system.(16,20) The concatenation of historical events affect CAS and the way in which external factors integrate into the open and dynamic system.(5,21) Our respondents reported the interplay of social history with clinical trial outcomes and future trust in research, showing that it is insufficient to assume independence of the social system from the clinical trial system.

To adequately address rumours, or better to prevent them, clinical trial design needs to acknowledge the emerging CAS that occurs when researchers enter a community. This extends beyond the initial introduction of the study and into the feedback sessions following the conclusion of the research. This will impact both clinical trial outcomes and future trust in research as rumours can be a reflection of the community's sense of dependence and inequality in relation to the clinical trial, expressed in familiar ways to the community.(3,16,22) A few respondents in our study expressed an awareness of this dependence and inequality. Highlighting the need for more to be done for the communities in which they are working, "*you cannot just collect data and forget about them*".

The kaleidoscope of feedback loops that are a part of the dynamic interactions within the CAS can make the identification of rumours and their roots difficult, however acknowledging this complexity and its consequences is necessary to strengthen clinical trial design. This can begin by identifying the rules which govern feedback loops related to rumours and to the historical roots out of which they have arisen. This can then be utilized for stronger community relations through communication about the vaccine by targeting these aspects specifically as a research team within the CAS.(23,24)

Beyond historical events which influence the CAS, introducing new and unfamiliar components into a system can also create unpredictable and non-linear outputs in the system. Within CAS, the outcome of an intervention can be major with what seems like a small situational change.(12,13) Researchers reported the challenge of introducing a new injectable vaccine study into the community, particularly when it is the first clinical trial taking place of this magnitude.

The inherent quality of CAS is unpredictability, in part due to the numerous feedback loops and networks interacting. For instance, the sensitization process around introducing a new vaccine could be further complicated by the presence of external research institutions conducting different studies, as was reported by respondents. The clinical trial is embedded in the social system but also open to the external environment. These external factors have an influence the CAS and aligns with three attributes that Cilliers (1998) assigns to CAS: *i) complex systems are open systems, ii) complex systems consist of a large number of elements iii) these elements interact dynamically*.(13) These attributes are also evident in the concerns raised about the introduction of a new HIV vaccine, where they highlight the importance of well-trained staff and a sensitivity to the local variations in

vaccination culture.(25) Other qualitative work in Kenya has also called for a greater emphasis to be placed on the norm sensitivity of health workers providing vaccine, as this is a way of identifying the rules of the CAS and thereby addressing the concerns as there emerge.(23)

While CAS outcomes are non-linear and dynamic, patterns of interconnections and cultural concepts emerge in each community, which impact the acceptance of a new vaccine. (25,26) Work looking at introducing a new human immunodeficiency virus (HIV) vaccine also emphasizes the importance that staff is prepared to adapt to new contextual settings.(25) Respondents often spoke about the role of local staff who were well-versed in cultural norms as well as the importance that the rest of the research team is aware of the community sociocultural values. Being embedded in the community and viewing it through the lens of complexity theory enables clinical trial researchers to better understand the rules governing the cause and effect within the local context.(27) However, operating in this way within the community is not without challenges.(28) The dispute that respondents described of a staff member losing their employment and subsequently contributing to circulating rumours or a politician using social events to gain support through discrediting the trial can be the consequences of being embedded in the communities in this way. The balancing of the clinical trial domain and everyday community life is challenging and requires a careful mediation that is open and searching.(28,29) Within complexity theory, these reported events are known as the *butterfly effect* where small changes in the initial system have major emerging implications.(11,30) The simple act of a community member losing their job due to not meeting the requirements, had implications on the trial as a whole and resulted in the spread of rumours that impacted the emerging image of the trial – an unpredictable, minor event that created ripples in the larger system as a whole.

The unpredictability and non-linear nature of CAS described above makes clinical trial research in low-resource settings challenging. The social system in which the research is carried out must therefore be integrated into the study design and not simply viewed as a single element of the clinical trial system. In addition to being aware of the cultural values and norms which influence the rules of the CAS, the hierarchy of the system is relevant to these rules as well. CAS are systems that have a hierarchy of power.(5) Central to the mediation within communities are the leaders, having a strong influence on the system as a whole. Respondents reported them contributing to the overall acceptance of the trial and also as having the power to create suspicions around blood draws if these hierarchal structures are not respected. Community leaders in Kenya have been identified to use their authoritative power to promote clinical trial acceptance or generate suspicion, depending on their perception of the research team.(31) Being aware of this hierarchy within the community will support researchers by equipping them with the ability to better understand the rules governing the feedback loops and networks within the community and the emerging patterns.

By integrating the above learnings into community engagement practises, vaccine clinical trial design can better embrace the unpredictability inherent to research in human communities. As the merging of a clinical trial and the community form a CAS, researchers working in any clinical trial that is embedded in a human community need to have the tools to be dynamic and adaptive to local realities. Designing a clinical trial with components of iteration

and reflexivity in synergy with the regulatory requirements will equip researchers to better adapt to the emerging behaviour that is inherent to all social clinical trial systems.

Conclusions

In this study we have identified the behaviour of a clinical trial system upon the merging with a human community. The factors identified by our respondents, as seen through the lens of complexity theory, are integral to informing how clinical trial research can be tailored to the local social setting. This expands into all clinical trial research operating in human communities. Prospectively, this pushes clinical trial design to incorporate iterative practices that adapt to the feedback loops and emerging behaviour of the clinical trial.

Here we have identified the key role that complexity theory plays in improving clinical trial design. Further research investigating other clinical trials and geographical settings through the lens of complexity theory is needed. This can build a consensus on specific system behavioural patterns that most heavily require an iterative focus by the clinical trial team. Through the establishment of these patterns a more standardized approach can be used to design iterative steps into any clinical trial.

Abbreviations

CAB	Community Advisory Board
CAS	Complex Adaptive System
GCP	Good Clinical Practice
HIV	Human immunodeficiency virus
SU-IRB	Strathmore University IRB

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the local ethics body, Strathmore University IRB (SU-IRB). All participants provided written consent to participate after being informed of the study details.

Consent for publication

Not Applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

MV and MT conceptualized the paper. MV wrote the first draft. MV, SM analyzed the interview data. SM, BO, NS, NBA and MT reviewed and provided substantial input into the revisions. All authors read and approved the final manuscript.

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Figures

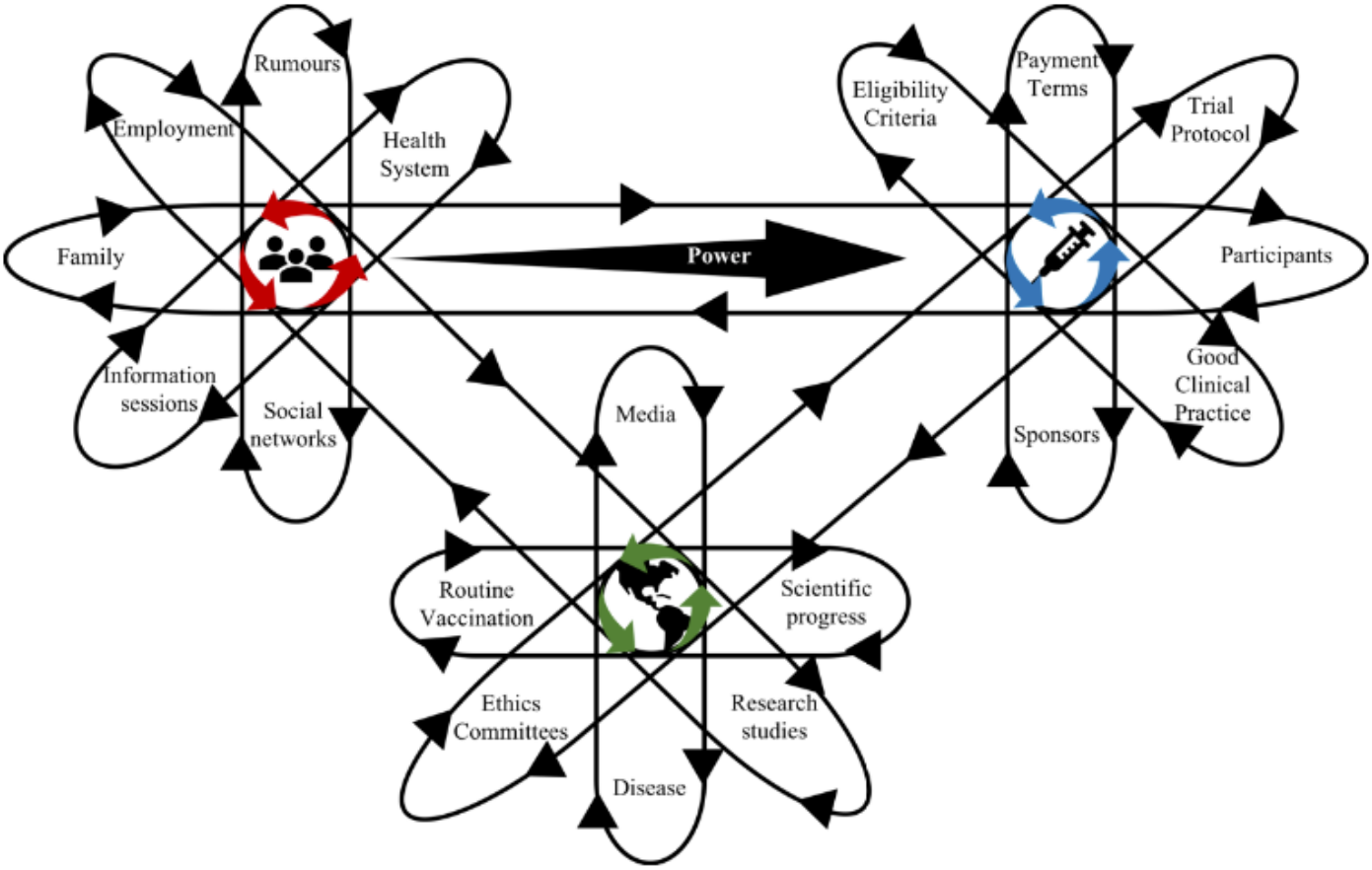

Figure 1

Complexity theory modeling a community system (red), clinical trial system (blue) and the external environment (green) merging into a new iterative system. The identified factors operate within feedback loops and demonstrate an interconnectedness with each actor. The solid arrow indicates the directional weight of power in the system, which is significantly greater on the side of the clinical trial.

Supplementary Files

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