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EDITORIAL

Rare disease research powered by empowered patients: solving the zebra puzzle through social media

Plain Language Summary

- Social media platforms like Facebook and Twitter have revolutionized rare disease research and have catalyzed the connection among patients with rare cancers.
- A new study from the Germ Cell Tumor Survivor Sisters Facebook group provides evidence of the utility of naturally forming patient groups assisting researchers with developing the evidence base for care and supporting those living with the disease.
- Such studies are the first steps in rare disease research powered by empowered patients by solving the zebra rare disease puzzle through social media.

The global burden of rare diseases that include rare cancers are increasingly becoming an enormous public health burden as they collectively affect an estimated 263 million–446 million people.[1,2] Because these rare diseases are geographically dispersed, it is quite challenging to conduct clinical trials on them. Until recently, major academic centers of excellence where these rare diseases are treated were the only hubs where expertise existed, information was available, trials were conducted, and patients were followed.[2] In most cases, clinicians and researchers got together once a year in a national meeting (if a society was created for that rare disease) for each of these rare diseases and shared scientific and clinical information. Patients and family members had to travel long distances and sometimes move cities to live near these centers. This created an immense emotional, societal, and financial strain on the resources of the families. Moreover, because the symptomatology of the disease and side effects of standard-of-care or novel treatments are unique to patients, it was difficult for patients to go through their journey with the disease alone. Historically, information about these so-called zebras (rare diseases) was sparse and remained an unsolved puzzle (Figure 1).

The new era of oncology social media has revolutionized rare disease research and patient groups like no other platform in the recent past.[3] Social media may not just be a place for researcher/clinician-to-clinician communication anymore. A true patient-centered approach of oncology means that we need to not only consider the patient but also have them involved in the development of trials and beyond. Many patients and health care professionals use social media to communicate about health issues with the potential of improving outcomes.

CAN WE IMPROVE PATIENT-TO-PATIENT INTERACTIONS WITH RARE DISEASES?

There are several key uses of social media for health communication among patients with rare diseases. Patient-to-patient communications breaks open silos, increasing interactions among patients with similar diseases, expanding the available information, widening access to more all-round health information, and last, more shared information brought to the forefront means that quality of life issues may be addressed. Moreover, for these rare disease patients who go through the disease journey alone, it has opened up a major avenue of peer-to-peer/social/emotional support. Increased communication among patients on comparing treatments and supporting each other in their treatment journeys can have a bearing on how patients feel.[4] When peer-to-peer social media data are collected and collectively analyzed, it can lead to major implications in public health surveillance and an enormous potential to influence public health policy for these rare cancers. With more information, patients and caregivers are empowered to make critical decisions. Social media platforms like Facebook and Twitter have catalyzed the connection among patients in closed groups of rare cancers and open forum discussions of rare diseases. For the clinician and researcher, this patient-reported data can lead to a deeper understanding of the life experience issues and toxicity issues beyond what is captured in trials. Although patient-to-patient interactions are well recognized in the field, the role of patient-to-researcher bidirectional interactions offers the possibilities of research that was previously unimaginable. Is this feasible and doable? In this issue of *Cancer*, White et al.[5] have provided the evidence that social media can help understand the treatment experiences of survivors of a rare cancer.

Granulosa cell tumors (GCT) are a group of rare diseases amounting to 2%–7% of malignant ovarian cancers.[5] There is an adult subtype characterized by *FOXL2*^{C134W} mutation and a rarer juvenile earlier onset subtype that does not harbor this mutation.[5] Although standard-of-care chemotherapy-based treatments exist, there is a gap of randomized clinical trial evidence with chemotherapy in

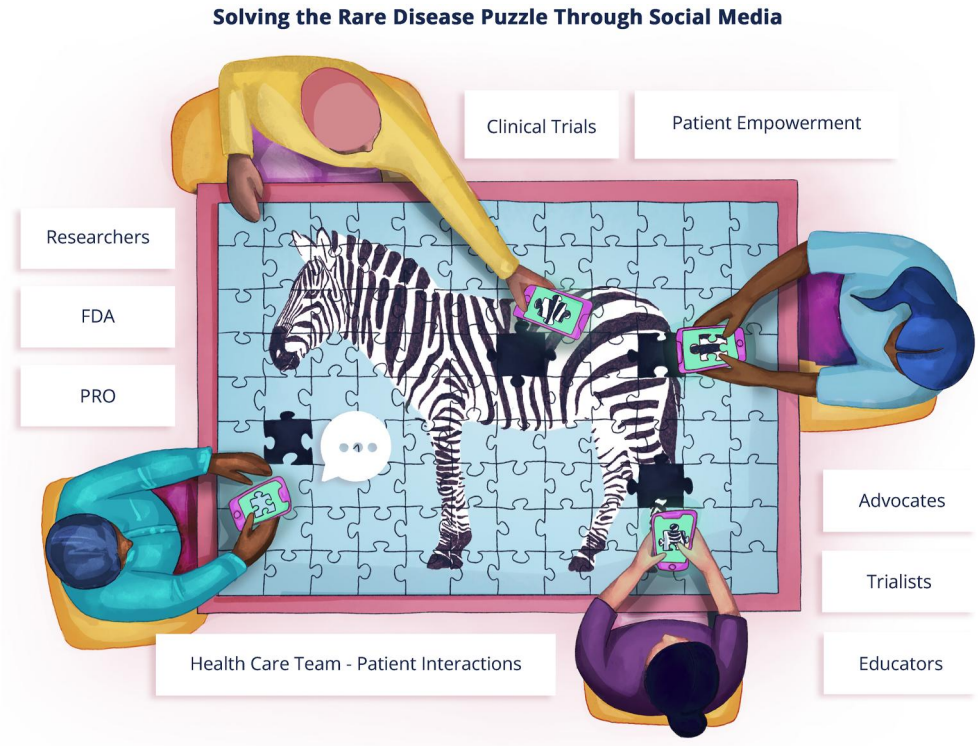

FIGURE 1 Solving the rare disease zebra puzzle through social media. Patients with a rare disease in diverse geographic locations across the globe inter-connected through social media trying to solve the rare disease puzzle.

early-stage and late-stage disease. The GCT Survivor Sisters (GCT-SS) Facebook group, comprises >1600 member participants from across the globe. The GCT-SS links together all survivors to provide support and information to adolescents, young adults, and women with both juvenile and adult GCT. The GCT-SS group has now formed a dynamic collaboration with researchers to advance research with the ultimate goal of improving the outlook for survivors with this rare cancer. White et al.[5] report the findings from the analyses of the collaboration between members of the GCT-SS Facebook group and researchers to assess member's experiences. This GCT-SS data set recounts the diagnosis, treatment, and follow-up care experiences of those with GCT and explores feasibility of "patient and public involvement" in data collection.

In this study, White et al.[5] reports 743 members (52 with juvenile GCT) with 67% stage I cancer at diagnosis that completed an online survey. The results of the survey revealed that treatment patterns were mostly aligned with clinical audits and standard-of-care, with 95% undergoing surgery and 19% adult GCT receiving chemotherapy. Recurrent disease was registered in 30% of patients and those recurrences occurred within 5 years of diagnosis for 33%. Some limitations of the study include a survival bias because only data from members who survived were collected and a sampling bias of younger patients who tend to be more active in social media channels. Because these are self-reported treatments on survey, verification of actual regimens was not undertaken, and this survival calculation is not possible because dates of diagnosis and recurrence were not available.

The authors must be commended and applauded for designing, executing, and reporting this innovative patient-powered research as one of the largest data sets assessing experiences with treatment and follow-up. It also may be one of the few studies to use a patient-public involvement approach for data collection.

Since its inception, social media has had a large potential in clinical research, becoming an important source of research because more than 4.48 billion people use social media. The future of social media and research is exciting when it comes to clinical trials because it has the ability to help in one of the biggest hurdles of clinical trials—patient recruitment, especially for rare diseases. There has been documented evidence that clinical trials can be augmented by social media, increasing the enrollment, allowing for a shorter recruitment timeline, and decreasing the cost.[6] However, adoption of standards for reporting recruitment and enrollment are necessary. With telemedicine expanding, the use of social media in these trials could in turn lend itself to more access through tele-consults and virtual clinics. One of the biggest advantages of the use of social media in clinical studies is the possibility of reaching marginalized populations that we would have otherwise not reached. Among these are many patient advocates who have not only the ability to engage with researchers, but also be part of the formation, design and condult of trials.

Many participants of studies do not want to simply be enrolled but would like to be involved in trial design and implementation of recruitment approaches.[7] This has the prospect to help in the evolution of recruitment of rare as well as common diseases. This

"patient centric" approach could lead to more support and enrollment. Patient communities have been formed in social media, some have even structured themselves to provide quantitative outcome data and are able to conduct observational studies. Social media can speed up clinical trials by enhancing patient access, patient engagement, and may even help lower cost.

Although these studies cannot replace the evidence from randomized control trials, the data could be used to speed up clinical innovation and control how well current treatments work. For example, there have been reports of researchers developing an algorithm to decipher the online behavior of patients with terminal diseases like amyotrophic lateral sclerosis (in the website PatientsLikeMe) on self-experimentation with lithium carbonate.[8] This analysis led to the same conclusion from a randomized controlled trial.

However, there are several drawbacks of social media—although it breaks open silos, it can also create more silos of multiple streams of information (or misinformation) from social media platforms (Facebook or Twitter). Where do we bridge the gap to make sure both physicians and/or scientists and patients are on the same platform, and who is the ultimate moderator?[9] Another pitfall is the digital divide (age and money as a hinder to participation). Although there is promise of patient-driven research to achieve their completeness, they require the collaboration of all researchers and cancer care providers involved. This would aid in a fuller picture when it comes to the diagnostics, tests, pathology, and molecular information. There needs to be constant monitoring for quality and reliability, all the while retaining the user's confidentiality and privacy. There are also a wide range of ethical challenges that come to social media recruitment and this is the reason this kind of recruitment must be planned rigorously, always taking into account the target group, the appropriateness of the SoMe channel, and the available resources to get this done.[10]

We are still in the very early stages of realizing the full potential of social media research in rare cancers. This report by White et al.[5] provides evidence of the utility of naturally forming patient groups assisting researchers with developing the evidence base for care and supporting those living with GCT ovarian cancer. Such studies are the first steps in rare disease research powered by empowered patients by solving the zebra rare disease puzzle through social media (Figure 1).

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