Improving Patient Involvement in the Drug Development Process: Case Study of Potential Applications from an Online Peer Support Network

Amrutha Anand, MPH; Helen Jane Brandwood, BSc (Hons); and Matt Jameson Evans, MA, MBBS, MRCS

HealthUnlocked, London, United Kingdom

ABSTRACT

To date, social media has been used predominantly by the pharmaceutical industry to market products and to gather feedback and comments on products from consumers, a process termed *social listening*. However, social media has only been used cautiously in the drug development cycle, mainly because of regulations, restrictions on engagement with patients, or a lack of guidelines for social media use from regulatory bodies. Despite this cautious approach, there is a clear drive, from both the industry and consumers, for increased patient participation in various stages of the drug development process. The authors use the example of HealthUnlocked, one of the world's largest health networks, to illustrate the potential applications of online health communities as a means of increasing patient involvement at various stages of the drug development process. Having identified the willingness of the user population to be involved in research, numerous ways to engage users on the platform have been identified and explored. This commentary describes some of these approaches and reports how online health networks that encourage people to share their experiences in managing their health can, in turn, enable rapid patient engagement for clinical research within the constraints of industry regulation. (*Clin Ther*. 2017;39:2181–2188)

Key words: online peer support network, patient centricity, patient voice, social media, user generated content.

INTRODUCTION

The Phenomenon of Social Media

Social media facilitates the sharing of information, experiences, and ideas among groups of people across the world with access to an internet connection. In an analysis of global digital users performed in 2017,[1,2] >3.77 billion people were found to use the internet, which indicates a 50% penetration (ie, the number of people using the internet as a percentage of total global population). Of this, 2.8 billion people are determined to be active social media users. These rates were similar to those reported in the Pew Research Center's Spring 2015 Global Attitudes survey.[3] The annual growth has followed an exponential trend in the past year, with a 21% increase seen in social media users from 2016.[1]

The Functional Evolution of the Internet

In addition to its user growth, the internet has come a long way functionally since its inception as a worldwide bulletin board system for sharing of messages, software, data, and news. It evolved to include company web pages and e-commerce during the explosive period of corporate growth between 1995 and 2001.[4] The recent evolution into an internet dominated by social media can be seen as a return to its initial utility as a peer-to-peer medium for exchange of information and news. Hence, social media has taken the internet full-circle back to a peer-driven system, but one that is ubiquitous and influential. Notably, social media is different from Web 2.0 (a platform where users continuously modify content in a collaborative manner) and user-generated content (all forms of media content created by and available to users); in fact, social media builds on Web 2.0 and allows creation of user-generated content (Figure 1). The key elements of this computer-mediated technology are the social presence (which

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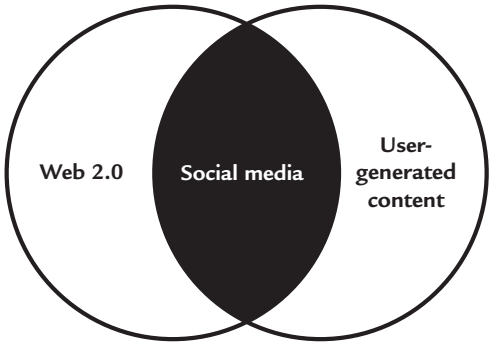

Figure 1. Social media as a confluence of features of Web 2.0 and user-generated content.

is linked directly to social influence) and the richness of content (which determines the effectiveness of the communication).

The pervasiveness and utility of social media in health and well-being are no exception. With high levels of consumption and sustained engagement, social media opens up venues for introducing online interventions that affect health behaviors.[5] The popularity of Facebook has facilitated many health behavior research studies in different populations with varying demographic characteristics and on a wide range of health behaviors, including weight loss,[6–10] physical activity,[11–16] and smoking cessation.[15] This medium allows for research to be conducted in private groups via polls or through apps on the platform. Twitter has also become a popular source of improving social engagement and has enabled the analysis of text within this medium to examine population-level health needs and behaviors.[5,17,18] Beyond the broad social networks, online patient communities and networks for health have allowed users to share information in dedicated, disease-focused networks, allowing them to log their experiences regarding their health. Furthermore, the anonymity and security offered by a peer environment have emboldened more people to be open about their struggles and challenges in managing their health.

Slower Uptake in Drug Development Research

In the first part of this decade, social media played a largely commercial role in targeted areas of the drug development cycle. In 2014, a White Paper[19] published by Tufts Center for the Study of Drug Development discussed and reviewed the use of social and digital media in clinical research. It noted that social media was used largely to market products and to gather feedback from consumers, with very few examples that supported clinical research. The same White Paper provided recommendations for patient recruitment and retention, development planning and study design, and adverse event reporting through communities on social media. In addition, patient-reported content has been used in the pharmacovigilance step of the drug development cycle for detection, assessment, understanding, and prevention of adverse events related to drugs, but there is a trend of underreporting these adverse events in postmarketing surveillance systems.[20]

This article takes a view, 3 years on, of how social media and peer networks have evolved to play a much deeper role in innovation and clinical research in industry and how the use of an online health platform's underlying semantic data structuring and artificial intelligence in its early stage is changing the opportunity for patients to participate in research and development of new therapies.

The Next Wave of Patient Involvement

We use HealthUnlocked.com (HU), a health social network with >40 million global visitors from August 2016 to August 2017, to provide a range of examples to illustrate how direct patient engagement in drug development through social media has evolved since 2014. These include examples include the following: involving patients in designing clinical trials, recruiting and screening patients into trials, running longitudinal research studies online, planning new drugs based on patient need, and surveilling the use of drugs and adverse events following launch into the market. These areas of patient involvement highlight how the role of the patient in drug development is changing significantly from the very early stages of exploring a new molecule through clinical trials and then the eventual launch of a new compound.

Methods developed to improve patient involvement in the drug development cycle included obtaining informed consent from all participants as standard protocol. The user was presented with a consent form that outlined the purpose of the research, research

partners involved, possible benefits and potential risks of participation, compliance with data protection acts, and privacy and confidentiality of shared data. In addition, members were notified that any content created on the platform is owned by HU and could be used for research purposes, although users could choose to opt out in their account settings.

CASE EXAMPLES

Clinical Trial Recruitment

A well-documented problem that pharmaceutical companies and clinical research organizations (CROs) face when setting up clinical trials is finding enough patients to send to site for assessment and randomization. With more commissioned clinical trials,[21] increased regulatory pressures,[22] and greater need for drug differentiation,[23,24] the demand for recruitment and retention of patients into studies has never been greater. Traditionally, recruitment has focused on the pull of health care professionals that patients may visit as an intermediary in the process. Study sites have mostly invested in above-the-line advertising, such as television or radio advertisements, or relied on physicians to remember relevant trials and match them with suitable patients they may see from day to day in a time-pressured environment. A commonly used analogy in industry is a needle in a haystack.

Recently, industry (pharmaceutical companies and CROs) has started using online sources to find patients for clinical trials.[25] Social media platforms, such as Facebook, are being used to recruit for clinical trials, and CROs are commonly building study-specific websites, allowing patients to find out more about the trial and contact details if interested in enrollment.

HU has attempted to support clinical trial recruitment by using its vast and diverse audience, where >4 million people access the platform each month and visit communities focused on 180 different conditions. Using the underlying artificial intelligence system, specific types of information can be gathered from user narrative texts to help target opt-in screeners to patients with a likely match for a clinical trial based on their condition, location near a trial site, and other factors. Use of the targeting technology means that a pull from physicians can become a push request[26,27] from patients to learn more about the trial by visiting their physicians.

For one such project, HU recruited patients for a trial that targeted a specific subgroup of patients with asthma. HU targeted users visiting the asthma communities from locations within traveling distance of the study sites. Patients were then led to a screener, approved by the sponsor and the relevant central and local institutional review board and regulatory bodies, to understand whether they may be eligible. This screener provided further information about the trial, the opportunity for patients to confirm their asthma diagnosis and meet additional inclusion and exclusion criteria, and the opportunity to be contacted by the trial site at a time slot suitable to the patient.

During 6 weeks, HU presented a pop-up or advertisement that introduced the asthma clinical trial >300,000 times to users, resulting in >3000 clicks to learn more and almost 1200 people attempting the screener. Overall, HU identified >85 patients in the United Kingdom and United States who met the screener criteria and were interested in learning more about the clinical trial and provided contact details to be put in touch with sites. The process from initial pop-up impression to the end of the screener could be completed within 10 minutes. The volume of users and the rapidity of progressing from one stage to the next is shown Figure 2. All patient information was kept strictly confidential, and data were stored on secure servers that support Health Insurance Portability and Accountability Act requirements. All information, including patient contact details, was transferred to study sites via encrypted files; no other identifiable patient information was shared with the sponsor.

Providing patients with more information and awareness of clinical trials can allow increased control over their own health and treatments. In addition,

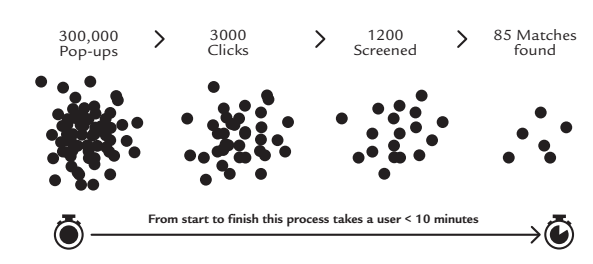

Figure 2. Flow of stages in clinical trial recruitment as observed.

recruiting via social networks also enables them to receive more detailed information about the trial through discussions with site staff on dedicated online communities. Even if eventual assessments determine they are not eligible, these communities can increase awareness of study sites and future opportunities for recruitment.

However, the beneficial effects of engaging prospective or existing clinical trial participants can stretch beyond the individual patient or healthy volunteer. For the study sponsor, every day of delay experienced in getting the final patient randomized can represent many millions of dollars in lost revenue. Being able to reach high volumes of a particular patient profile so swiftly offers a paradigm shift in reducing recruitment timelines and consequently provides a greater window of patent protection.

Furthermore, by systematically engaging patients through a digital platform, valuable insight for the whole health care industry can be gleaned around patient preference with regard to trial participation. These insights can be used to inform trial design and improve recruitment and retention—balancing demands on the patient with patient-centered value propositions (eg, setting of care) and ancillary support (eg, transportation).

Rapid Insights to Design Trials

Although pharmaceutical companies are planning trials to ensure that the highest regulatory standards are met, the patient experience is often forgotten, despite it being one of the most critical factors to ensure a successful trial. Some CROs and pharmaceutical companies are now realizing the importance of the patient voice and are actively trying to make trials as patient-centric as possible, including involving patients in the trial design, making the measurements meaningful to patients,[28] actively engaging with patients to improve dialogue about clinical trials, and supporting them through increased education and awareness. Patient advocacy groups and social networks are being used to relay patient insights and feedback into drug development process.[28]

An example of a social network collecting patient insights to affect the drug development process is involving users via HU. The quick and easy access to patients provided by the platform means it is possible to gather information about patient motivations, concerns, and opinions on clinical trial designs. Understanding these motivations can affect the design and running of a trial. HU worked with INC Research to better understand areas of opportunities for creating more patient-centric trials. For example, key concerns of patients were used to optimize recruitment (eg, understanding the symptoms bothering patients with lupus revealed that 83% considered their quality of life and work activity were affected by their disease. Specific countries or regions with high interest to participate in clinical trials were identified to redirect site resource to maximize recruitment (eg, 72% of surveyed patients with lupus in Latin America were interested in taking part in a clinical trial compared with only 39% in Europe). Targeted recruitment efforts were possible by understanding the clinical specialty that most commonly treated patients (eg, 54% of patients with chemotherapy-induced neuropathic pain were treated for the pain by their oncologist, with none of them visiting a neurologist). Methods to make the clinical trial process as patient-centric as possible were developed to affect recruitment plans (eg, 39% of patients with early-onset Alzheimer disease and their caregivers indicated they would be more likely to take part in a clinical trial if travel accommodations were made, such as taxi or car service or hotel stay). As well as initial trial enrollment, these measures could extend their effect on patient retention rates.

All patient information was anonymized, and no contact information was retained.The extensive HU audience across geographic and disease areas means that it is feasible to gather >100 responses in a short time (ranging from 2 days to 2 weeks). The availability of this information at such short notice can be vital for study teams in the fast-moving study setup and bidding process.

Patient Insights Relating to Drug Delivery Design

Traditionally, patient preferences have been obtained via interviews or face-to-face focus group discussions, and even these would be constrained by geography and prevalence of the patient segment. However, in recent years, online resources are being considered as ways of actively or passively understanding patient needs and preferences.[29]

Using the HU social network, a pharmaceutical company identified and recruited a segment of users to be part of an online focus group. The focus group was tasked with concept testing a range of formulation types, with the broader aim of improving acceptability

to patients and, in turn, drug adherence. Online recruitment efforts reduced the time to recruit and removed the geographic constraints of a focus group with fixed location. Using underlying artificial intelligence, patients who were likely to benefit from different formulations were targeted based on semantic inferences from their discussion or browsing pattern. Targeted patients were invited to learn more about the study and complete an eligibility screener, which allowed an online focus group to be populated with 40 patients within 28 days. During screening, demographic information was captured to ensure inclusion of representative samples.

A private, online community was then set up on HU, where a number of questions and exercises were conducted during the study period. Privacy meant all responses were protected from public access and there was no response bias. In addition, all patient information collected was kept strictly confidential and was stored on secure servers that support Health Insurance Portability and Accountability Act requirements. Anonymized data were not shared with the sponsor.

After enrollment, research questions were posted into the research community of 40 patients during 2 weeks. The second week of questions were largely centered around feedback on the formulation concepts. Participants were initially asked to provide feedback via private message to ensure reduced bias before taking part in discussions with other participants as a group exercise. Polls were also posted to get quantitative data, alongside the extensive qualitative data. The final results were analyzed based on the age and sex of participants.

The online community produced unexpected, insightful, and considerate responses from participants. The 2-week research period allowed participants time to consider their responses and put together detailed, thoughtful answers. It also allowed for the evolution of thoughts and ideas as they ruminated on the subject. Interaction with other participants on the discussion posts prompted brainstorming with discussions that led to the evaluation of opinions and ideas during the research. The opinions and experiences of others greatly affected how participants thought about the questions, taking into consideration factors that they had not experienced themselves.

For the participants, this online approach allowed them to remain anonymous while being part of a group discussion. For the pharmaceutical company, patient perspective was assembled with reduced logistical complications and at a lower cost versus traditional offline tools.

Adverse Event Reporting

Pharmacovigilance is a crucial domain in the drug lifecycle in which online peer to peer networks can shed light. With >1 million data points in a network for any specific health condition, there is an abundance of user-generated content available for examination of valuable insights. Armed with statistical, machine learning, and linguistic techniques, it is now possible to closely explore unstructured text entered by users of online health communities and derive meaningful insights from them.

HU collaborated with an academic research partner to develop pilot studies to assess the feasibility and validity of extracting insights from user-generated data. One such concept is the identification of beneficial and adverse effects of steroid use in patients with rheumatoid arthritis. Constructed on the MATTER method developed by Pustejovsky,[30] a sample dataset of user text from an online health community for a particular health condition will be used to annotate various phrases and texts, building a manually curated dataset that can further be used to train an algorithm. After this, the algorithm is then tested over a larger dataset, evaluated for reliability, and revised to improve the robustness of the annotated dataset. Although simple, the entire process involves manual review of data by a team of experts (clinicians and researchers) building complex algorithms to assess natural language and rounds of revisions to improve the whole data mining tool.

Moving ahead in this domain, there is a concept being developed to flag adverse reactions to drugs or medical instruments and procedures solely from unstructured user content on online health communities, which will then automatically alert the regulatory agency.

Studying Patient Behaviors and Adherence After Launch

Medication nonadherence varies with patient characteristics, diagnosis, and treatment regimen among other factors, and these rates have been found to be as high as 60% in some instances.[31] Nonadherence is most prevalent among patients who are symptom free or undergoing treatments aimed at prevention and among elderly patients, all of whom may escalate to

nonadherence.[31] Nonadherence negatively affects patients, physicians, and the entire health care system by limiting the benefits of medicines, which could result in the deterioration of a person's health, in turn increasing the burden on the system. In the long run, it causes both personal and economic losses.[32] A prescribed solution to improve overall medication adherence rates in the population is empowering patients to have better interactions with their physicians, to feel motivated to stick to their medication regimen, and to be involved in their treatment plan to have a clear understanding of the need for each medicine.

As part of an impact study, HU evaluated the effects of online peer support on its users using the Patient Activation Measure (PAM),[33–37] a validated instrument that measures a person's level of activation,[38] defined as the knowledge, skill, and confidence in managing one's own health. PAM has been extensively peer reviewed and is considered a gold standard to measure self-management abilities. Higher levels of activation have been strongly linked to better clinical outcomes, reduced health care service use, and better experience with treatment through adoption of healthy behaviors and improved medication adherence.[39] This validated questionnaire was administered twice (with a follow-up period of 3 months) through an online survey to members of communities on the social network platform. The results from these survey responses were analyzed along with users' online behavior metrics. A total of 31% of respondents were seen to move up the activation scale during the follow-up period, and as a result of this increase in score, a significant increase in medication adherence was expected.[40] Because the concept of activation is not condition specific and most socioeconomic conditions have limited effect on it, it is possible to improve the activation levels of users and sustain these improvements to have an effect on medication adherence.

CONCLUSION

The notion that patients should be involved in key decisions across the whole drug development cycle is increasingly commonplace throughout the pharmaceutical and clinical research industry. The internet, in particular, the mass adoption of social media platforms, has opened the door to the involvement of patients directly, rapidly, and on an ongoing basis.

The 2014 Tufts Center Social Media White Paper reported a lag in the use of this opportunity as mainstream practice in drug development, and the regulatory and operational constraints of the health care industry were recognized as a barrier to adoption. Since 2014, however, there has been a noticeable shift in adoption alongside the evolution and sophistication of tools and techniques that are provided from social media to industry. In particular, the mass mobilization of patients into disease-focused online communities, such as HU, allows a cohort of patients to participate in drug development as a group that also enriches their lives through involvement.

In a 2017 survey of 2079 HU users, more than half (60.8%) were interested in taking part in clinical trials, and 40.5% were interested in taking part in market research. This interest may enable industry to make better decisions: "To truly engage with patients, we must understand what makes them tick," says Clare Grace, vice president, Site and Patient Access at INC Research/inVentiv Health. "The rich insights we were able to gather in collaboration with Health-Unlocked open the door to designing successful trials and accelerating the delivery of important therapies to patients."

A definitive shift in the process of improving patient involvement is yet to be observed, but with defined and tested methods and strong partnerships with industry, academia, and patient groups, online health networks such as HU can have a significant effect on bringing the patient voice to the forefront.

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CONFLICTS OF INTEREST

All authors are employees of HealthUnlocked. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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Address correspondence to: Amrutha Anand, MPH, HealthUnlocked, First Floor, Clover House, 147-149, Farringdon Road, London EC1R 3HN, United Kingdom. E-mail: amrutha.anand@healthunlocked.com