
Article:
Hanchard, M. orcid.org/0000-0003-2460-8638 (2022) Issue-networks as omitted publics in the construction of #rarediseaseday discourse. Wellcome Open Research, 7. 276.

https://doi.org/10.12688/wellcomeopenres.18433.1

RESEARCH ARTICLE

Issue-networks as omitted publics in the construction of #rarediseaseday discourse [version 1; peer review: awaiting peer review]

Matthew Hanchard

iHuman Institute (Social Sciences), University of Sheffield, ICOSS, 219 Portobello, Sheffield, S1 4DP, UK

v1 **First published:** 09 Nov 2022, **7**:276
https://doi.org/10.12688/wellcomeopenres.18433.1
Latest published: 09 Nov 2022, **7**:276
https://doi.org/10.12688/wellcomeopenres.18433.1

Abstract

Background: Over 450 million people worldwide have a rare disease. Yet despite healthcare policy rhetoric placing an onus on inclusive public engagement, rare disease publics are often engaged as data sources or product/service consumers. Meanwhile, various rare disease actors congregate around 'Rare Disease Day' each year – a global event with various online and offline talks, workshops, and sessions. In 2021, ~4.3 million tweets marked Twitter as a locus of exchange for the event.
Methods: To examine public discourse around the event, the paper draws on social network and qualitative analyses of 40,366 Twitter tweets/retweets about rare disease day 2021 posted between 10-Feb-2021 and 10-Mar-2021, analysing them through a controversy theory lens. After identifying particularly influential Twitter users and groups, the paper examines their textual and visual communication strategies.
Results: It funds three distinct orientations to rare disease discourse on Twitter (mission, awareness, and actor). In doing so, the paper locates a gap in direct engagement between medical authority and patients.
Conclusions: It suggests that each orientation towards the discourse around rare disease day 2021 might be used by policymakers and researchers to engage with rare disease publics on social media in a more inclusive way as a pathway to better healthcare provision.

Keywords

Health communication; Rare diseases; Public engagement; Social media; Sociology of health and illness; Social network analysis

Open Peer Review

Approval Status *AWAITING PEER REVIEW*

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Matthew Hanchard (m.s.hanchard@sheffield.ac.uk)

Author roles: Hanchard M: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This research was funded by the Wellcome Trust as part of a project held by Professor Paul Martin, titled: Orphan drugs: high prices, access to medicines and the transformation of biopharmaceutical innovation [219875].
The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

How to cite this article: Hanchard M. **Issue-networks as omitted publics in the construction of #rarediseaseday discourse [version 1; peer review: awaiting peer review]** Wellcome Open Research 2022, **7**:276 https://doi.org/10.12688/wellcomeopenres.18433.1

First published: 09 Nov 2022, **7**:276 https://doi.org/10.12688/wellcomeopenres.18433.1

Introduction

Rare disease policy in both the EU, UK, and USA promotes public engagement. By contrast public understandings of rare diseases are often informed by social media interactions between patients, family and carers, and patient organisations. This is especially the case during global events like rare disease day. However, discourse generated on social media around rare disease remains largely unmapped, leaving questions open about which actors and/or groups of actors are influential in shaping those public understandings, and how they do so i.e., who gets to shape which narratives around rare diseases are foregrounded or silenced, and via what textual and visual strategies. Addressing these questions is important in understanding how rhetoric around public engagement in rare disease policy plays out on social media, and how well aligned discussion surrounding rare diseases are with it. To address these questions, in the article below I draw on issue-mapping as an analytical framework (Marres & Rogers, 2005; Marres, 2015) and apply it to Twitter data. Through a social network analysis (SNA) of 40,366 tweets/retweets about rare disease day 2021, I identify Twitter users with high in/out degrees and closeness/bridging centralities as the most prominent actors shaping communication around the event. I also find that they tend to form discernable issue-networks as communities bound by a shared orientation in terms of their narratives and identity. Following the SNA, qualitative analyses of tweet/retweet content within each issue-network enables me to draw out the textual and visual communication strategies they each employ.

The article starts by highlighting the importance of rare disease day as a locus for online rare disease discussion worldwide. It then looks at policy rhetoric around public engagement in rare disease policy before highlighting its antimony with the lived experience of patients not being engaged with via social media. With this background context in place, I turn next to controversy analysis literature (issue-mapping in particular) to lay out an analytical lens before introducing the data and methods it has been applied to. The latter combines SNA with qualitative applied thematic analysis. Three finding sections follow, through which I identify separate issue-networks around amyotrophic lateral sclerosis (ALS), lymphangioleiomyomatosis (LAM), and various aortic dissection related diseases (AD). After examining the overall shape of each issue-network and the relations it encompasses including prominent actors/groups, I analyse their re/tweet content. This involves focussing on textual and visual communication strategies employed to define the issue-network boundaries and identities, and the narratives promoted. Overall, I find three orientations in the Twitter discourse around rare disease day (mission, awareness, and actor), each defined by a particular set of communication strategies. Across them, the article finds a lack of engagement by medical authorities and regulators. Thus, the article argues that the latter ought to engage with patients on their own terms via social media as a means to more inclusive and meaningful form of public engagement and knowledge exchange, with rare disease day as key site for doing so.

Rare disease day 2021

Every year, on the last day of February, the US-based umbrella patient organisation NORD organise and host a global event called 'rare disease day' (Hanchard, 2021a). The event provides space for dialogue, exchange, and awareness-raising about 6,000–8,000 known rare diseases (Yáñez-Muñoz, 2017) affecting ~450 million people worldwide (McMullan *et al.*, 2021). Through various talks, workshops, exhibitions, meetings, and performances the event brings together a diverse and globally dispersed array of rare disease communities. In 2021, a majority of the event was held online for the first time (Rare Disease Day, 2021). This was partly due to coronavirus restrictions on travel and public events as well as the potential risk posed to individual attendees' health (Ibid.). As a publicly open and conversational medium (Bruns, 2012) which enables easy interaction between a broad range of actors around a key topic (Walter *et al.*, 2019), Twitter quickly took centre-stage, garnering ~4.3 million tweets about the event in a single month. This afforded Twitter potential to enable "individuals, grassroots movements, and political and social elites to directly communicate to the public and influence [their] opinion" (Münch *et al.*, 2021, p. 1). However, to date there remains a dearth of research to date on social media discourse around the event.

Public engagement rhetoric in rare disease policy

Rare disease policies often place an onus on public engagement (Bauer, 2017; EMA, 2020; HM Govt, 2020). For example, in the UK, there is a focus on "[e]ngagement and dialogue with the public, patients and our healthcare workforce, [by] placing the patient and the diverse UK population at the heart of this journey" (HM Govt, 2020, p. 7). This is notable in UK national rare disease strategy, which places a firm focus on engagement via a rare disease forum (HM Govt, 2022). Across the EU, a European Medicines Agency (EMA) initiative similarly involves engagement with 'patients' and 'healthcare professionals' as broadly defined categories (EMA, 2020). Meanwhile, the US Food and Drug Administration (FDA) goes further in setting a formal strategy of participating in Rare Disease Day by holding "Face to Face meetings with patient advocacy groups" at the event (Bauer, 2017, p. 15). All three territories follow a shift from "one-way normative notions of public understanding of (i.e., deference to) 'science', [on] to the supposedly two-way [dialogic] public engagement" (Wynne, 2007, p. 100) in deciding what counts as legitimate/illegitimate knowledge in more diffuse and democratic ways (Voss, 2019). However, under a broader shift towards public engagement, these policy decisions are often framed by a perceived need to 'educate' the public by priming levels of acceptance and tolerance for risk - set against a fear that doing so may entice activism and direct protest (de Saille & Martin, 2018). As a result, medical authorities often treat "user-generated content of social media sites as little more than backchannels [that] …spread misinformation, [meaning that] communication has been mostly one-way, from departments to the public" (Keller *et al.*, 2014, p. 2). Thus, in practice, public engagement is steeped in medical authorities' preconceptions over which

publics to include/exclude (de Saille, 2015) and researchers' one-way elicitation of patient accounts. Despite the promise of social media, in practice this means medical authorities' public engagement often involves patients being treated either instrumentally only as sources of data and/or as treatment consumers. At the same time, patients and their mobilisation into patient organisations has seen both dialectically "depend on medical expertise in the development of scientific research with diagnostic and prognostic objectives [whilst they also] challenge [the] social, cultural, economic and often politicised dominance of medical authority in health decision-making." (Vicari & Cappai, 2016, p. 1654).

Patient interaction on social media

Speaking at the World Orphan Drug Congress 2021, Kimberly Richardson, advocate leader for Ovarian Cancer Research Alliance (OCRA) noted that the main point of contact (and therefore main source of information) for ovarian cancer patients (rare or otherwise) are clinicians - who in turn stringently follow policy and research recommendations (McKee & Richardson, 2021). She also stressed the potential for public engagement to go beyond treating patients instrumentally and/or using testimony of living with a disease to reaffirm known anthroprographics and/or risk factors. Instead, she urged instead for a more sustained dialogue between researchers and patients to forge new symbiotic relationships. Within this line of reasoning, "social media [might] allow individuals to quickly obtain, generate and disseminate information… making medical knowledge more accessible to all and fostering health consumerism" (Valente *et al.*, 2022, p. 2). That is, social media might offer a useful avenue for disseminating understanding of the science behind rare diseases and their treatments. Thus, it could better educate patients whilst offering researchers valuable information about patient experiences as a meaningful form of knowledge exchange. However, Richardson recalls a recent project where researchers seeking ovarian cancer patients via a large advocacy organisation stalled when they found that patients had not been broken down into subtypes. Meanwhile, a social media group with >1500 members was gathered and ready, with patients self-sorted into subtypes, many of whom would have relished the chance to engage with the research. Despite an invitation by the Facebook group, no contact was made by the researchers. Here, Richardson argues that employing social media for recruitment and dialogue could help researchers and clinicians alike to generate more "meaningful relationships with their audiences, [and] develop more dynamic and detailed research questions" (McKee & Richardson, 2021). Extending this, Mesko and deBronkart (2022) posit that a 'paradigm shift is underway in the patient-clinician relationship, driven by irreversible changes in information access' across the healthcare section. In this, a better understanding of the social relations involved with the construction of public knowledge via social media is becoming increasingly important.

Controversy analysis and issue-mapping

As an analytical framework, this paper follows Hanchard (2021a) by drawing on Marres and Rogers' (2005) notion of 'issue-networks' and its parent literature controversy analysis; both broadly understood as digital methods research (Rogers, 2013). Originally, Marres and Rogers examined connections between webpages, arguing that "the sender of the link 'frames' the site of the receiver, as it presents the link under a particular heading, or as part of an overview" (Marres & Rogers, 2005, p. 1). Here, issue-networks are composed of "heterogeneous set[s] of entities (actors, documents, slogans, imagery) that have [been] configured into [a] hyperlink-network around a common problematic" (Marres & Rogers, 2005, p. 6–7). They add that this enables research "to go beyond the loudest voices and binary oppositions, [and] to reveal the multisidedness and intersectionality of social media controversies" (Burgess & Matamoros-Fernández, 2016, p. 93). Extending this, Marres and Moats (2015) draw on Bloor's (1982) notion of symmetry, whereby actions are understood in the wider context of those not taken, beckoning researchers to "set aside true and false and treat all positions as scientifically viable. Doing so reveals that all sides have to make arguments that include a socio-political dimension" (Marres & Moats, 2015, p. 2). As such, they urge researchers not to focus on a priori categorisations, but to open themselves to a broad range of actors and their relations with a reflexive awareness of potential connections being left latent.

Applying the above lens to the research means treating social media both instrumentally (as a data gathering tool) and as an object of study in itself by "elucidating [the] dynamics specific to [studied] digital media platforms" (Marres & Moats, 2015, p. 5). This involves an interdisciplinary approach, with "digital techniques [used] for the capture, analysis, and visualization of – often Internet-based – data to render legible disputes about public issues" (Marres, 2015, p. 658). Here, as Marres notes, controversy analyses can either: a) aim to separate 'legitimate' from 'illegitimate' knowledge claims; b) be discursive in seeking to "detect relations between substantive arguments and socially and politically located actors and to render such relations available for interpretation by various audiences…by analyzing which claims and issue terms have support from which actors" (Marres, 2015, p. 661); or c) they can be (radically) empiricist, "with researchers making no decisions on the site of study upfront in order to seek to minimize ontological assumptions" (Marres, 2015, p. 663). In this article I take a discursive approach. First, I follow a hashtag and search term through social network analysis (SNA) to examine how different actors congregate around particular controversies to form issue-networks. I then examine the content of re/tweets circulating within particular issue-networks through an applied thematic analysis (Guest *et al.*, 2014).

Data and methods

Study design

The paper draws on an accompanying open access dataset (Hanchard, 2021b). The research behind the dataset began with an exploratory analysis of the term 'rare disease day' and hashtag #rarediseaseday in Twitter, using social network analysis (SNA) to do so. For this, all data were gathered between 10-Feb-2021 and 10-Mar-2021 covering tweets posted

between those dates (inclusive). It identified a core set of vocal and influential Twitter users. It also quantified their relative importance in shaping public understandings of rare disease. The SNA found that specific groups of users (issue-networks) are important arbiters of knowledge within particular controversies around rare disease. It also found an absence of engagement from medical or regulatory authorities. The research then turned to qualitative applied thematic analysis (ATA) of tweet content within those issue-networks to identify a set of communication strategies. In combination, this research design addressed research questions about: (1) which users and/or groups of users are the most prominent in shaping discussion around rare disease day on Twitter; (2) which users and/or groups of users' garner the most interactions (i.e., the highest number of retweets, quotes, replies and/or comments); 3) the communications strategies employed by the most prominent groups of users; and 4) how regulatory and medical authorities feature and relate to prominent groups within the construction of rare disease discourse.

Data collection

Data were gathered via DMI-TCAT, the University of Amsterdam's Digital Methods Initiative (DMI) Twitter Capture and Analysis Tool (TCAT) - available at https://github.com/digitalmethodsinitiative/4cat. The tool that queries Twitter's STREAM API, stores the results on a local MySQL database, and then outputs them as a .CSV file (Groshek *et al.*, 2020). Twitter's API restrictions mean that DMI-TCAT can only offer a 1% random sample of all tweets on a query (Gerlitz & Rieder, 2013). However, this sample has been found to be both generalisable (Groshek & Tandoc, 2017) and "relatively proportional" (Groshek *et al.*, 2020). DMI-TCAT also "closely follows Twitter's information structures, abating Marres and Moats' (2015) concern over the framing potential of data gathering tools. The dataset (Hanchard, 2021b) for this article comprises a node and edge list with 40,366 nodes, representing a 1% random sample of all tweets/retweets posted between 10-Feb-2021 and 10-Mar-2021 containing either '#rarediseaseday' and/or 'rare disease day'. In temporal terms, 92.62% were posted between 27-Feb-2021 and 03-Mar-2021 and none before 24-Feb-2021, with a 31.66 mean average daily decrease after 03-Mar-2021. Tweets were typically retweeted only a few times (M 2.46, SD 17.35) with 853 receiving direct replies and 32,856 garnering mentions. Thus, the sample depicts an ephemeral flurry of communication around the event with very little pre-emptive build-up and swift dissipation afterwards. Also, a shallow communication flow revolving primarily around retweets, mentions, and quotes rather than any meaningful or invested two-way dialogic conversations. This made it sensible to examine who tweeted most (vocality) and who was mentioned/quoted most (influence) through SNA before interrogating tweet content through ATA for qualitative insights. It also highlighted the centring role of rare disease day as an event that elicits a 'coming together' of various rare disease communities for a short time only, marking it as a prime potential avenue for public engagement by medical authorities.

Ethical considerations

The paper draws on an open access dataset (see the *Data availability* section below) deposited onto the University of Sheffield data ORDA repository on 26-Aug-2021. In-line with ethical approval granted by the University of Sheffield Research Ethics Committee on 02-Jun-2021 (approval number: 039187) the dataset entailed written informed consent being obtained directly from participants/patients to cite their Twitter content and/or to use either their real Twitter username or a proxy pseudonym - with the exception of public figures acting in a public capacity.

Social network analysis

All SNA were conducted in hi version 0.9.3[68] which rendered the data into a network with 24,600 unique nodes (Twitter users) and 48,891 edges (tweets/retweets, and/or mentions/quotes/replies). In analysing the data, some measures provided a general overview of the network as a whole: *average weighted degree*, for instance, depicted the average number of edges per node (tweets/retweets per user) across the network. Meanwhile, *average path length* showed how many Twitter users a tweet passed through (i.e., via retweets) on average between sender and recipient, and *diameter* depicted the longest possible path between any two nodes in the network.

A second, more granular set of measures related to individual nodes rather than the whole network, providing "effective entry points for further qualitative research" (Felt, 2016, p. 8). For example, *in-degree* offered each node a relative score between 0 (none) and 1 (highest in the network) based on how many edges pointed towards them i.e., how many times a user's tweets/retweets were interacted with by others (including likes, comments, replies and retweets). Its counterpart, *out-degree,* offered a similarly relative score (between 0 and 1) based on a node's outward interactions i.e., how many times a Twitter user interacted with the tweets of other users. The two in/out-degree figures enabled specific nodes (Twitter users) to be identified as being more/less prominent and/or vocal than others – both across the network and within specific clusters (discussed below). Likewise, *bridging centrality* serves to identify nodes that act as 'bridges' connecting nodes along a specific path and/or that tied together separate clusters. As a related measure, *closeness centrality* 'is based on the idea that nodes with a short distance to other nodes can spread information very productively through the network' (Landherr *et al.*, 2010, p. 2) and can be calculated as the average path length of a node to all others in the network.

A third set of measures operated at a meso-level, revolving around community detection i.e., identifying clusters (groups) within the network. These ranged from dyadic clusters with just two nodes to giant ones incorporating a large portion of the network. For this, *modularity* was a key measure, which Gephi calculates using the Louvain algorithm (Blondel *et al.*, 2008). It first treats each node as a standalone cluster, comparing them across the network based on *in-degree* and *out-degree*

scores. It then calculates 'up to a multiplicative constant… [single-node clusters with] edges falling within groups minus the expected number in an equivalent network with edges placed at random' (Newman, 2006, p. 2). That is, when the inward and outward edges of a node (the tweets/retweets received and sent) connect it with another node or set of nodes more than any others *and* more than would occur at random – then a cluster is identified (as a type of community). Alongside this, *cluster coefficients* show how well/poorly individual nodes connect with one another within their cluster based on their inbound and outbound interactions (Hansen *et al.*, 2020). As a relative measure, the latter shows how strongly/weakly tied together clusters are.

All social graphs below (Figure 1 to Figure 7) use Gephi's force-directed layout called 'Force Atlas 2', designed by Jacomy *et al.* (2014). For Venturini *et al.*, this form of 'topological' visualisation offers an important avenue for exploratory analyses in as far as '[n]etworks are not only mathematical but also visual objects' (2021, p. 1). Thus, they enable SNA to provide not only detail on the measures discussed above, but also provide an overall 'grasp [of] more general relational patterns' (Venturini *et al.*, 2021, p. 13). Within the social graphs below the circles/dots represent nodes (Twitter users), each colored by their modularity class (cluster) and sized according to their in-degree or out-degree (i.e., larger nodes sent/received more tweets/retweets, smaller ones sent fewer). The lines represent edges between nodes and are colored by the tweet/retweet source (i.e., the originator of the tweet/retweet interacted with) with line thickness weighted relatively by out-degree score.

Applied thematic analysis

Following the SNA, an applied thematic analysis (ATA) of tweet/retweet content provided meaningful insights into the discourse circulating within prominent clusters (at the meso level). It also offered a way to differentiate between individual nodes being connected in clusters by cluster coefficients based on specific similarities (i.e., shared language) and discursively discrete ones that revolved around a particular topic as an

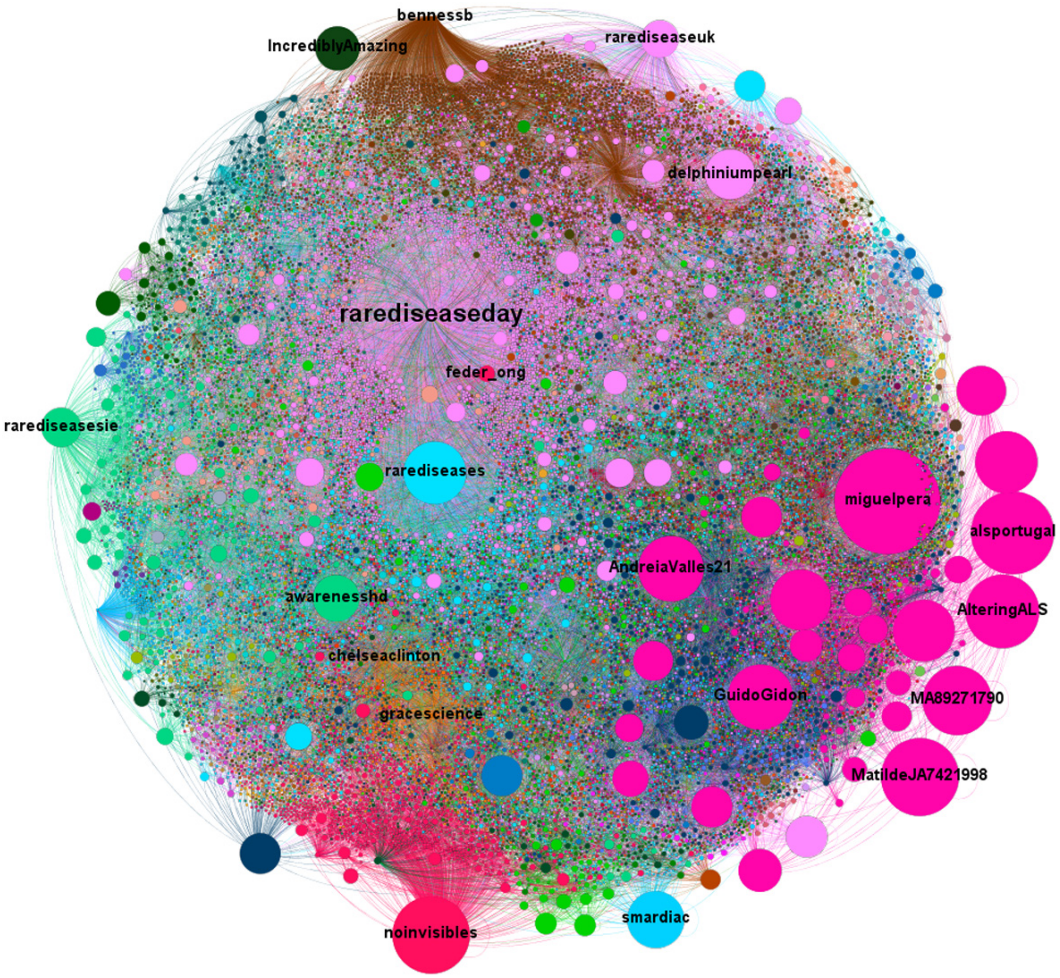

Figure 1. Social graph of vocality.

Figure 2. **Spanish language cluster (on tweets).**

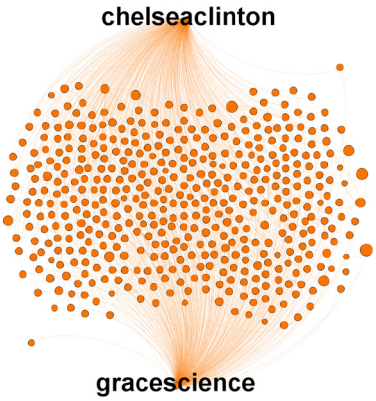

Figure 3. **Broadcast cluster.**

Figure 4. **ALS network.**

issue-network. This involved an in-depth reading of tweet/retweet content (text and images) through a three-stage process of: (1) generating initial qualitative codes; (2) whittling the codes

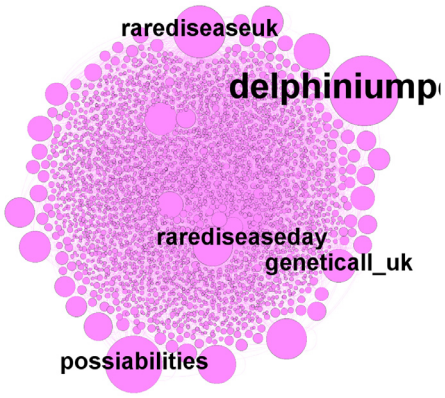

Figure 5. **LAM Network.**

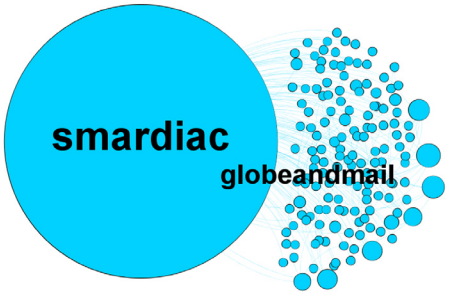

Figure 6. **AD Network.**

to more refined set; and (3) theorising them as themes (Guest *et al.*, 2014) drawing on controversy analysis concepts to do so. Within this, embedded media, mentions, and hashtags within tweet/retweet content were treated as the "entities to which the activities of users, bots, and platform algorithms converge and through which they mutually transform one another" (Omena *et al.*, 2020, p. 5) in working towards a shared orientation. Thus, whilst the SNA identifies clusters, the ATA (employing a controversy analysis lens) locates issue-networks amongst them and the orientations they congregate around.

Results

The role of users in shaping discourse

At the network-wide scale an SNA on Tweets showed various actors being vocal about rare disease (Figure 1). Their communication flowed through 6 retweets (the average path length) up to a maximum of 18 (network diameter), meaning that content passes through several intermediaries as retweets before reaching its final recipient. Tweets were typically retweeted or quoted only two/three times too (average weighted degree 2.47), with 1,103 modularity clusters indicating that a small set of highly visible users tweeted a lot (Table 1). This situated the network somewhere between a 'hub-and-spoke' (star shaped) and a 'polarized' structure (Himelboim *et al.*, 2017). Most of the clusters were small and ephemeral (574 were dyadic and formed around a single retweet). However, larger clusters formed around

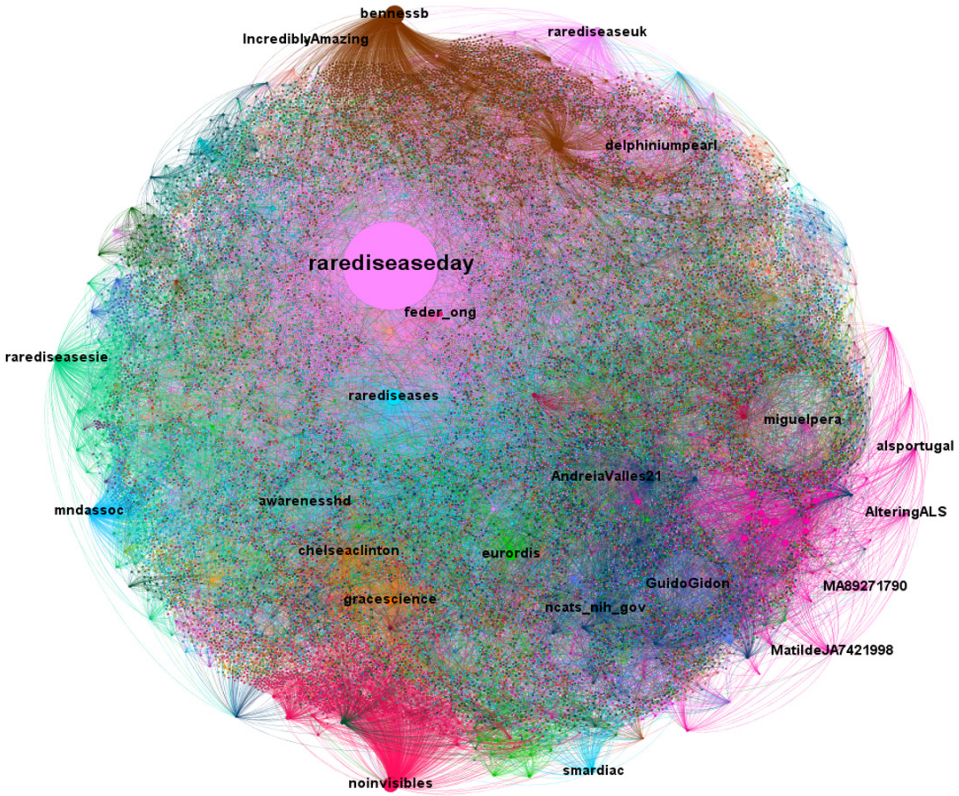

Figure 7. **Social graph of mentions.**

Table 1. **Fifteen most vocal users.**

User	Tweets	Followers	Mentions	In/out degree	Type
MiguelPera	369	371	0	0 / 81	Patient Group
AlsPortugal	288	547	0	0 / 69	Patient Group
MatildeJA7421998	270	199	35	21 / 50	Patient
Noinvisibles	268	48,948	851	682 / 57	Organisation/Platform
AlteringALS	255	861	5	5 / 51	Patient
MA89271790	239	126	56	27 / 34	Retweet bot*
AndreiaValles	226	80	14	14 / 49	Patient
GuidoGidon	226	72	0	0 / 40	Patient
RareDiseases	215	35,249	916	720 / 167	NORD
JulesDeol547981	215	132	0	0 / 45	Patient
Mirabella82676571	213	93	53	21 / 33	Patient
Eliana1678422	209	30	0	0 / 45	Patient
smardiac	195	358	41	12 / 129	Charity
delphiniumpearl	171	147	2	2 / 87	Retweet bot*
Mariana5457481	169	110	38	18 / 49	Patient

highly active mutually reinforcing users, i.e., one 458-user cluster formed around *feder_ong* (Spanish Federation of Rare Diseases) and *noinvisibles* (Spanish-language community rare disease charities). Their respective in-degrees of 132 and 682 (against a cluster mean of 2.05) and closeness centralities of 0.24 and 0.25 (versus a cluster mean 0.23 and standard deviation 0.21) also depicted the strength of their influence through reciprocal retweeting between two main nodes within the cluster. Rather than forming an issue-network, however, they united around a Spanish language audience (Figure 2). Similarly, a foundation that funds research on NGLY1 deficiency (*gracescience*) was retweeted by Chelsea Clinton (*chelseaclinton*), potentially reaching the public figure's three-million followers. Their clustering followed a single tweet to generate a broadcast-shaped cluster, not one coalescent around a sustained issue per se (Figure 3), but rather a temporary formation around a single high-profile tweet. Other highly vocal influencers like *IncrediblyAmazing* were isolated from the network (at the outer edge of the social graph). Their 150 tweets interspersed rare disease matters with the Texas power outages and Black Lives Matter protests. As a single-user cluster with an in-degree of 0, *IncrediblyAmazing* retweeted and mentioned others a lot, but saw no interactions with their own output. Thus, they illustrate the point that vocality does not always signify communication flow across networks.

Compared to the clusters described above, issue-networks were identified as taking a different form, with shared orientations centring around a particular concern. One 322-user issue-network surrounding ALS and advocacy for FDA approval of drug NurOwn, for instance, dominated the network as a giant cluster (Figure 4). It had few highly vocal users (e.g., *MiguelPera* and *AlsPortugal*), with others retweeting more than posting original content (Table 1). In a second issue-network, *delphinumpearl* is highly vocal amongst 3,884 users tweeting/retweeting about LAM (Figure 4). Their 171 tweets and out-degree of 87 against a cluster mean average of 2.78 (SD 6.59) highlighted the potential impact of a non-human influencer (a manually managed account with a retweet bot attached). Elsewhere, fully human-managed accounts like *rarediseaseday* (the official event account) and *possiabilities* (a rare disease content aggregation site) were equally influential, illustrating a diffusion of power across various users albeit centred by a shared orientation around religiosity. Their tweets also intersected with discussion of various rare diseases, not just one disease, leading to a less rigidly bounded issue-network than the ALS one (Figure 6). Elsewhere, *smardiac's* tweets about various genetic conditions related to AD culminated in a 149-user issue-network (Figure 6)with an out-degree 10.75 times larger than their in-degree (Table 1) positioning them as a central influencer i.e., they were typically retweeted, mentioned, or quoted 10 times for every tweet/retweet they posted.

In short, what the SNA above show are that issue-networks are constituted by various actors, but often marked by a subset of influencers who group together, and who are important to the flow of communication about individual rare diseases and rare disease day in general. Within this, policymaking and research institutions tweeted very little, contributing minimally to public discourse about the event on Twitter. For example, the EU Commission, National Institute of Health, NHS England, and University of Oxford (*EU_commission*, *NIHDirector*, *NHSEngland*, and *UniofOxford*) all tweeted about rare diseases only once during the month surrounding rare disease day 2021. Instead, discourse primarily revolved around interactions between patient organisations and individuals. This highlights a significant disparity between policy rhetoric around public engagement and its practical enactment, opening questions about who influences online discourse around rare diseases, what strategies they employ, and the role of various mediators.

The role of most-mentioned users in shaping discourse

Extending the analysis above to an SNA on mentions revealed overlap between vocal and highly mentioned users, with several network features mirrored between them. However, there were differences in how users clustered together, where there were 1,098 weakly to 23,249 strongly connected components across the same 1,103 clusters (Figure 7), indicative that only a few influencers dominated in most clusters - albeit with limited interaction i.e., the 15-most mentioned users rarely retweet each other (Figure 8).

Twitter users within each cluster of the SNA on mentions were more diverse than they were for vocality based on Tweets. That is, although *rarediseaseday* received the most (8.37%) mentions, the next five most mentioned accounts included a podcast host, charity, two patient organisations (POs), and an individual patient (Table 2). Their numbers are, however, artificially inflated at times. For example, *bennessb* and *sugismundposts* retweet each other regularly in mutual reinforcement (Figure 9). Elsewhere, clusters closely aligned with the vocality SNA, with the Spanish-language cluster re-appearing for instance, but with *noinvisibles* significantly more influential than *feder_org* (Figure 10).

The three issue-networks identified above (ALS, LAM, and AD) reappeared around mentions too, but held slightly different shapes (Figure 11). The ALS one contained a dominant subcluster of 13 highly influential users with >200 mentions each (all others had <70). Amongst these influential nodes there was cross-over and exchange between a heterogeneous range of actors, including highly vocal patients (e.g., *MiguelPera* and *AlsPortugal*) and medical authorities – such as the FDA (*us_fda*), the European Commissioner for Health and Food Safety (*skyriakideseu*), and a pharmaceutical company specializing in neurodegenerative disorders (*amylyxpharma*). Their roughly equal number of mentions opened questions for the ATA about how these different actors interacted in the construction of rare disease discourse.

A less prominent set of users within each issue-network, many of whom fall outside the bounds of traditional consideration by policymakers and POs also helped shape discourse around rare disease. In the ALS issue-network this included *chelsienotes*, a writer, advocate, and ALS patient's partner.

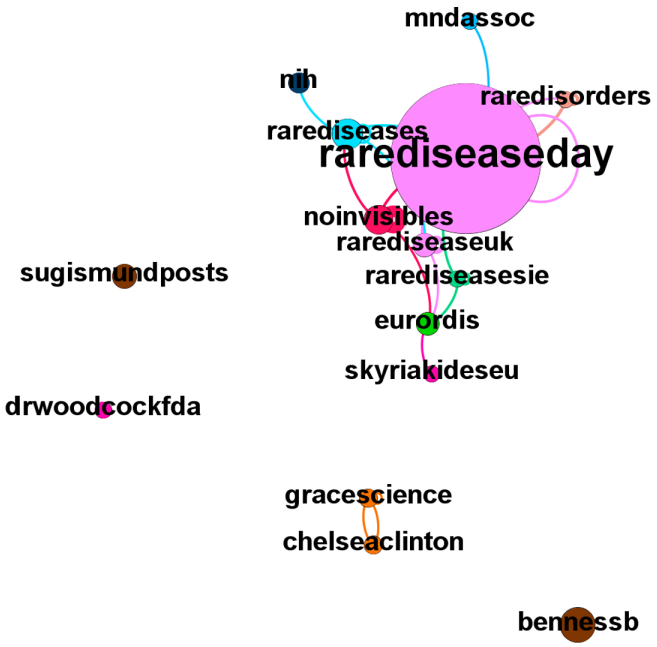

Figure 8. **Fifteen most mentioned users.**

Table 2. **Fifteen most mentioned users.**

User	Mentions	Followers	Tweets	In/Out degree	Comments
rarediseaseday	5709	35e,282	22	3953/19	Official event account
bennessb	1087	12,519	2	1081/2	Podcast host
rarediseases	916	34,899	215	720/167	NORD (event host)
noinvisibles	851	48,756	268	682/57	Organisation/Platforms
sugismundposts	670	704	0	663/0	Patient
rarediseaseuk	642	20,315	126	419/65	Charity (part of *Genetic Alliance*)
eurordis	596	26,114	2	495/2	Patient Organisation
nih	525	1,338,481	2	396/2	Medical authority
gracescience	425	1,120	2	423/2	Charity
chelseaclinton	421	3,008,935	1	418/1	Public figure
drwoodcockfda	367	9,291	0	60/0	Medical authority
skyriakideseu	350	49,960	7	92/6	Medical authority
rarediseasesie	348	3,122	133	218/88	Charity
mndassoc	345	35,227	1	344/1	Charity
raredisorders	340	4,312	53	255/26	Patient Organisation

Also, digital activist *bethmccarthy2004*. With in/out-degrees of 41/0 and 14/0 respectively they tied the issue-network together (with closeness centralities of 0.57 and 0.15 respectively). Users often interacted with their tweets to shape discourse in a particular way – even though they were not highly vocal themselves (i.e., their few posts were widely retweeted).

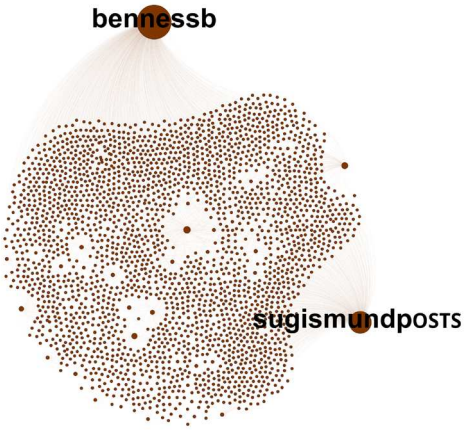

Figure 9. Mutually reinforcing users.

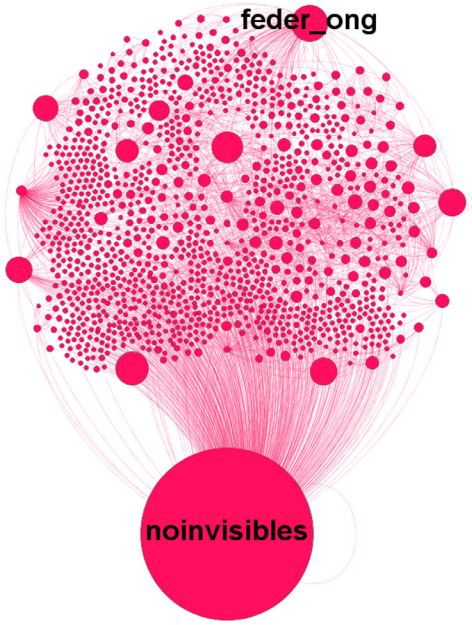

Figure 10. Spanish language cluster (on mentions).

Together, these findings highlight a diffusion of power in issue-networks around mentions that differs from vocality, in which the range of users considered influential can be broadened.

This argument followed into other issue-networks. In the LAM one, highly vocal users such as *delphiniumpearl* and *possiabilities* remained important to communication flow - even if *rarediseaseday* is mentioned disproportionately more. There was permeability too, with users like *ehlersdanlosuk* mentioned by users both inside and outside the issue-network following their separable tweets/retweets about LAM and Ehlers-Danlos syndrome (EDS). Furthermore, in the AD issue-network, rather than *smardiac* being the primary node and thus the key influencer (Figure 3a), the issue-network splits into two subclusters in the mentions SNA connected by *globeandmail* (a Canadian national newspaper) – a node with a bridging centrality of 0 but a bridging coefficient of 1.68 – that ran a story about a fundraising event organised by *smardiac*. Here, *Smardiac's* bridging coefficient of just 0.000061 sees *globeandmail* as relatively stronger in holding the two subclusters together. Meanwhile, *Smardiac's* exceptionality high betweenness centrality of 144,9202.31 saw the node as far more integral to tying together the overall issue-network as a whole.

In short, a broad range of actors were important for issue-networks to form around particular rare diseases on Twitter during rare disease day, not just highly vocal and frequency mentioned ones. Some had very little direct activity on Twitter (including many policymakers), with many acting instead as bridges. In addition, boundaries between issue-networks were found to be permeable to varying degrees. Thus, whilst assessing tweets and/ or mentions via SNA provided a sound basis for an exploratory analysis in identifying issue-networks and key actors, it did not provide the means to fully contextualise them. As such, it left questions for the ATA to address about how discourse is constructed differently within each issue-network and the strategies involved with its construction.

Discourse within and between rare disease issue-networks

Within the dataset, 16,343 (40.49%) of the sampled tweets contained hashtags and 22,820 (56.53%) embedded media (still or moving images), making a qualitative analysis of textual and visual content important for exploring their discourse. In doing so, an applied thematic analysis (ATA) of tweet content from users within the three issue-networks identified through the SNA (i.e., ALS, LAM, and AD) found that they each revolved around a particular orientation towards rare disease discourse (i.e., mission, awareness, and actor).

Mission-orientated discourse within the ALS issue-network. A Portuguese-language subcluster of the ALS issue-network applied gaudy green frames to their profile pictures with the surrounding text 'Lucha mundial contra la ela' (the global fight against ELA) as a shared brand identity. This followed users across Twitter, beyond the subcluster and issue-network boundaries in raising public awareness about ALS. To clarify, as a form of digital activism, it aligned with a Change.org (2021) petition (Figure 12) advocating for the approval and the 'right to try' *NurOwn* - an investigational drug then at phase one of clinical trials (BrainStorm, 2020; FDA, 2021). The issue-network coalesced around a particular disease, with a dominant subcluster intersecting with an ongoing campaign outside the platform around wider issues of access, pricing, patient choice, and risk about a specific rare disease drug all bound together through a brand identity.

This visual strategy recontextualized the text of issue-network members' tweets too. For example, when *AlsPortugal* retweeted *mcandrew10*, their framed profile picture reappropriated

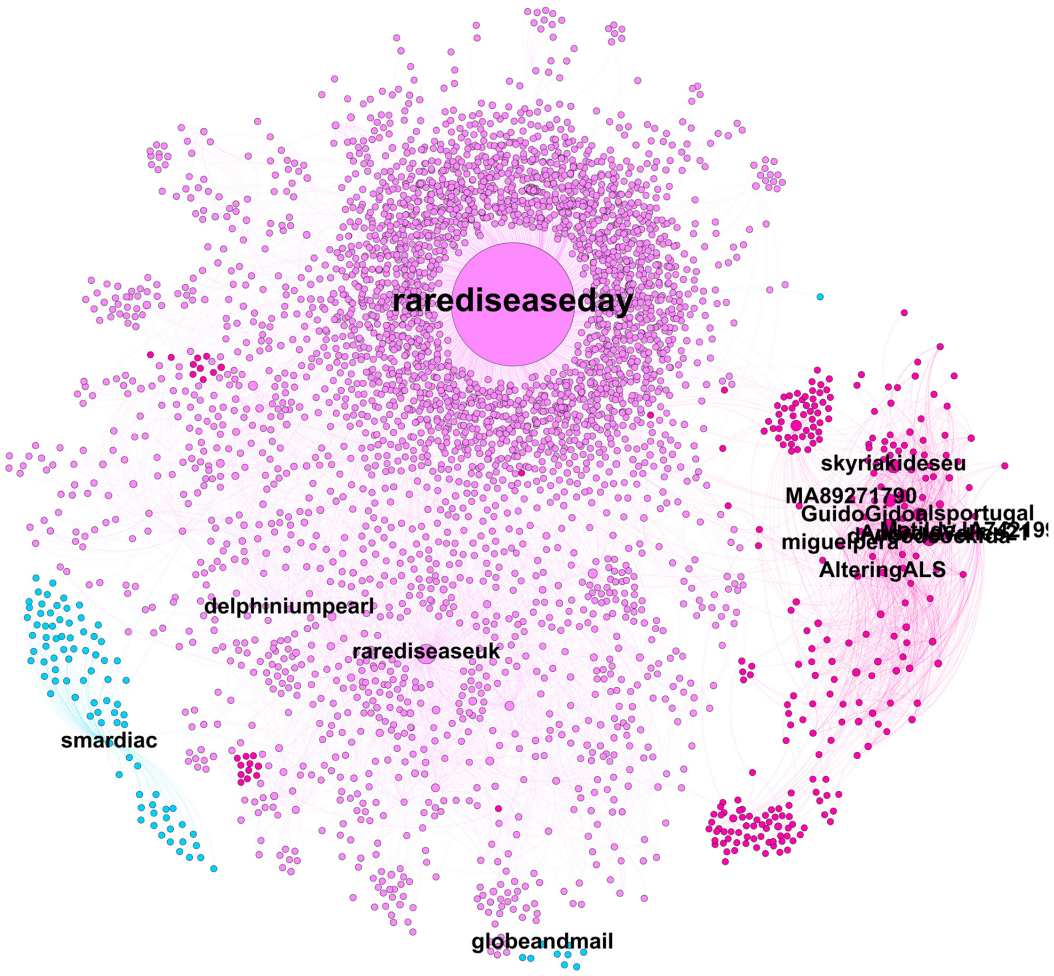

Figure 11. Three issue-networks (ALS, LAM, and AD) on mentions.

the original tweet, including its mentions and hashtags. Doing so strengthened the politics of advocacy in the original tweet by reframing it through a visual motif aligned with the dominant subclusters' brand identity:

> RT @*mcandrew10*: #RareDiseaseDay #RareDisease-Day2021 #alsawareness #NurOwn ##NurOwnNow @*FDACommissioner* @*US_FDA* @*DrWoodcockFDA* (https://t.co/YMC7bKS3Bp)

The original tweet hashtags referred to Rare Disease Day, ALS, and NurOwn, whilst mentioning the FDA and its Acting Commissioner of Food and Drugs. A composite image on the original tweet also combined the official event banner with an evocative personal photo of the user holding a placard stating 'I will change the world with my Father who is fighting ALS'. Here, *AlsPortugal* strategically reused *mcandrew10's* (English-language) tweet by putting it out to a (primarily) Portuguese-language subcluster within the same issue-network. Doing so served both to cement *AlsPortugal's* role as a key bridge for the issue network, following a in/outdegree ratio of 0 to 69 - albeit with a closeness centrality of 0.18 and bridging coefficient of just 0.01. It also enabled the issue-network to publicly engage with a major US institution and global audience. What their example illustrates is the linguistic and geographic fluidity of Twitter rare disease discourse. It also highlights how users support and draw on each other to strengthen their online advocacy in ways that resembles the mutual reinforcement found in other clusters. Underpinning both there is a visual rhetoric at play in using a uniform profile frame in a show of unity around a core concern, an approach that helps cohere the issue-network.

Others combined the ALS profile banner with hashtags at a geographically distinct scale. One tweet by *ALSEUROPE1*, for instance, used #ALS, #MND (Motor Neuron Disease) along with its Spanish and French counterparts #ELA (Esclerosis Lateral Amiotrófica) and #SLA (sclérose latérale amyotrophique). Combining these with mentions of the Euro-

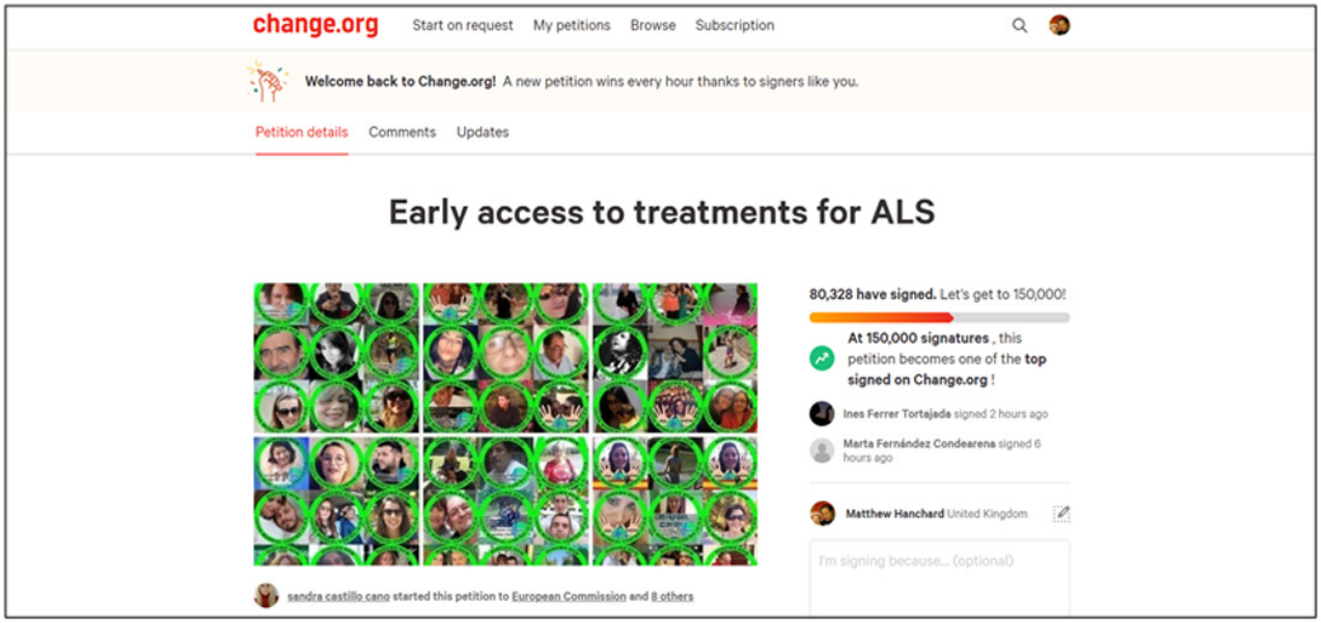

Figure 12. Screenshot of *NurOwnNow* Twitter profile picture banners on Change.org.

pean organisation for patients and professionals with ALS (*EUpALS*), European Commissioner for Health and Food Safety (*SKyriakidesEU*), and the European Medicines Agency (*EMA_News*) ensured the issue reached a broad set of Southern European audiences:

> An incidence=number of annual deaths is what makes ALS rare. 500k people are dying,1 every 90min. #ALS #MND #ELA #SLA need access to investigational drugs, therapies can't be stuck in research silos!100% fatal! #uhc4rarediseases @vonderleyen @SKyriakidesEU @EUpALS @EMA_News (https://twitter.com/alseurope1/status/1370699407050616834)

As part of this, *ALSEUROPE1* quantified the ALS deaths per year to strengthen their claim through empirical fact whilst asserting that therapies should not be 'stuck in silos' - a reference to the high-cost quandary troubling European policymakers (Denton *et al.*, 2021) and its impact on research progression, innovation, and patients' lives.

Irrespective of whether they aimed towards a geographically localised or global target, or whether they simply tweeted or reappropriated others' tweets, users' strategies within the ALS issue-network worked towards a particular mission (a form of coherence missing form most clusters); public awareness-raising, digital activism, and advocacy around the approval of the ALS treatment NurOwn.

Awareness-orientated discourse and the LAM issue-network. Compared to the ALS issue-network, others adopted less visuality-based forms of unity amongst their membership. The LAM one, for instance, followed a more awareness-orientated approach. Here. *delphiniumpearl* retweeted Japanese and English (dual language) content, making extensive use of tweets with embedded media. Aspirational photographs of nature and animations around wellbeing were interspersed with personal testimony and evocative videos about living with a LAM, often containing references to Christianity, including biblical quotes. In one tweet, for example, *delphiniumpearl* used the generic event hashtag (#rarediseaseday) whilst mentioning Our Daily Bread (a Christina charity) and requoting their 'question of the day' – in this instance taken from the Christian Bible's Book (ESV Online, 2001) of Lamentations (3: 19-26):

> #RareDiseaseDay "How has God sustained you through the trials you've faced? How could you support someone who's enduring a challenging time?" [LRI]@ourdailybread[PDI] (https://t.co/29DlZxUTfE)

This awareness-based approach paired with religiosity, when followed by others in the same issue-network, included more retweeting than direct tweets (notable in the average in-degree and out-degrees of 1.30 and 2.15 respectively) when compared the ALS issue-network, as well as less frequent use of hashtags. However, the use of religious references was not confined to Christianity alone. When *shahida_moosa* tweeted about their interview with Radio Islam International, it was retweeted six times and liked ten times. The interview involved a similar mission as *delphiniumpearl's* in raising awareness about LAM alongside other rare diseases, albeit whilst speaking specifically to a global Islamic community:

> Rare Disease Day 2021: Interview on Radio Islam International, jazakumAllah khairun to @AnnisaEssack & @radioislam for including me in your show today. Our community can do much more to support families

> with #RareDiseases. It is our privilege, our duty & our responsibility! (https://twitter.com/shahida_moosa/status/1365945529277050880).

Here, discourse was constructed in a similar way by communities surrounding different religions; both raising awareness of LAM through core influencers, drawing on embedded media and religious references as points of connection. Rather than awareness-raising for a particular mission or ethos (as the ALS issue-network did) discourse in the LAM issue-network was subsumed under a wider strategy of approaching rare diseases through notions of religion and community. Elsewhere, connection with the specificity of LAM as a disease was far more direct. For example, one *delphiniumpearl* retweet broadcast the American Thoracic Society (*ATSfellows)* to a wider audience:

> RT @ATSfellows: ATS summary of LAM for clinicians Link: https://t.co/v1KAMoYp6x 1. What is LAM? 2. Indications for sirolimus 3. Indications for VEGF testing 4. Avoid doxycycline and hormonal therapy (https://twitter.com/ICUCharts/status/1090957169611235330)

The original tweet contains a hyperlink to a summary academic article by Feemster *et al.* (2017), highlighting take-away points from a research project at the University of Washington. Doing so provided a spatio-temporally proximate reference point, rather than drawing on global religion-based communities. Nonetheless, the onus remained on public awareness-raising and information sharing. Tracing links from these users extended beyond the issue-network, further supporting the claim that the LAM issue-network is more dispersed and permeable than the ALS one. This is notable, for example, when the LAM foundation retweeted an event hosted by the US National Institute of Health's (NIH) Center for Advancing Translational Sciences (*ncats_nih_gov*), reaching audiences both within and outside the issue-network:

> RT @ncats_nih_gov: Today is recognized as #RareDiseaseDay around the globe, intended to raise awareness for #RareDiseases and improve access to treatments. NCATS and @NIHClinicalCntr invite you to join us virtually for #RDDNIH tomorrow on Monday, March 1. Register to attend: https://t.co/Z6K3AhwiwD https://t.co/hco3AGdTFL

Boundary-crossing tweets like this, however, held little strategy beyond being descriptive and/or informative, i.e., to advertise the public about an upcoming event. By contrast, the boundary-work of users like *delphiniumpearl* and *shahida_moosa* used religion, nature, senses of community, evocative imagery, and patient testimony to form a shared awareness-based orientation, forming brand identities for those users as highly retweeted influencers. This, the LAM issue-network held a core orientation at its centre with a more dispersed periphery. Leading to a less well-defined or bounded issue-network.

The AD issue-network and actor-orientated discourse. Much like the LAM issue-network, one identified around aortic dissection (AD) diseases revolved primarily around a small set of individual actors (human and non-human). For example, *smardiac* (Skinny Genes) was a Canadian charitable foundation run by a single person. They used photographic images, hashtags, and mentions strategically, and sported the foundation's bespoke logo as a profile picture. This provided a recognizable brand identity across all received mentions and retweets. Pairing this with an evocative profile bio, *smardiac* states their aim of "[r]aising awareness 4 genetic disorders causing aortic dissections. Turning tragedy into purpose after losing my dad to the #genetic disorder I was diagnosed with". Here, the hashtag #genetic ensures that the profile and its tweets reached a broad range of actors beyond rare disease day itself.

As part of their charity work, *smardiac* promoted a silent charity auction coinciding with US Heart Disease Month and Rare Disease Day, using hashtags to reference the Canadian-US National Hockey League (NHL) and US Centre for Disease Control (CDC). As such, their 28-Feb-2021 tweet aimed at audiences specific to rare diseases (heart-related and otherwise) alike:

> Today is #RareDiseaseDay! Please check out my fundraiser, bid on one of the amazing items up for auction, and donate to help me in my mission to save lives! #NHL #HeartMonth (https://t.co/637jrghL8a) (https://twitter.com/smardiac/status/1366081373413367811)

Although the tweet provided limited detail of auction items (for lack of space), it did offer a hyperlink inviting viewers to open a webpage about the event – located on the website of a local newspaper called the *Trail Times* (see Bailey, 2021). The website, then, serves as a non-human member of the issue-network situated outside Twitter, referencing (and thus directing) its readers to the Skinny Genes foundation Twitter account whilst providing expanded detail on auction items. In another tweet, *smardiac* noted that all auction proceeds would fund "a Scholarship I've set up in my Dad and Uncle's name" (https://twitter.com/smardiac/status/1362478187716911108). Including the hashtag #NHL (National Hockey League) within the tweet broadcast this funding to an audience far wider than the issue-network, highlighting the importance of both *smardiac* and the NHL in shaping the AD issue-network's geography as primarily Canadian and North American. Here, rather than focussing solely on fundraising for the auction, *smardaic* continued to be highly vocal, tweeting in for instance on 06-Mar-2021 that:

> Too many are living with these deadly genetic disorders and will never know until it's too late. I want to educate people around the signs and symptoms of these conditions; using the memory of those I've lost to help save others. Please donate below
>
> (https://twitter.com/smardiac/staus/1266381889423601666)

Other users in the AD issue-network shared this orientation. For example, *CMichaelGibson*, a medical doctor and Harvard Professor with heart disease specialism retweeted *smardiac's*

fundraising tweet, whilst remaining highly vocal about a broad range of heart diseases (including non-AD ones). Their accounts highlight permeability through the AD issue-network's boundaries, with members engaging both with AD and wider heart disease discourses, as well as referencing key actors as a strategic means to expand their network and drawing on key influencers as bridging nodes. Thus, the visual and textual strategies they employed were actor-orientated, and whilst often geographically localised, included a wide range of actors including those external to Twitter.

Conclusion

This paper has shown that Twitter users group together (in clusters) around rare disease day 2021 through shared language, around public figures and highly vocal/mentioned individual users, and by mutually reinforcing each other. It argued that some users coalesce into issue-networks around particular diseases and/or attendant advocacy concerns. Their activities often extend beyond Twitter and include external websites and/or events – a point on which a cross-platform study of social media discourse could usefully extend this paper. By identifying three rare disease issue-networks (ALS, LAM, and AD) and examining their strategies and discourse, the paper has highlighted three orientations (mission, awareness, and actor). Here, the use of visual motifs and hashtags to establish shared brand identities was identified as a key aspect of a mission-orientated approach, often localised to subclusters surrounding advocacy campaigns. Thus, Twitter is engaged for awareness-raising and digital activism with reciprocal retweeting used to strengthen claims. Other issue-networks were less firmly bounded, drawing on aspirational images of nature and/or religiosity, evocative media, and patient testimony to promote senses of wellbeing and community more globally. As such, Twitter affords public awareness-raising and community-building around rare disease without connection to specific campaigns. Yet other issue-networks revolve around a few highly influential users making strategic use of hashtags and mentions to promote and broadcast events. The latter often extended to include actors external to Twitter as part of an actor-orientated approach (i.e., newspapers and websites). In identifying these three orientations as different ways in which discourse around rare disease day has been constructed, the paper leads to suggestion that by engaging with social media as a key site of public discourse, and Twitter in particular, key policymaking institutions and researchers could adopt more targetted approaches to public engagement. Either by addressing specific influencers (identifiable through their high in/out degrees and closeness/bridging centralities), by making connections with religious communities as an entry into engaging with specific rare disease communities, and/or by tracking the advocacy concerns and debates within digital activism around particular campaigns (identifiable through specific hashtags). Doing so would yield useful synergies in engaging with rare disease publics (i.e., patients, carers, family members) in a more inclusive way. Meeting rare disease publics on their own terms in this way would generate space for two-way dialogue and knowledge exchange. It would therefore help align medical authorities' practices with their policy rhetoric about public engagement.

Data availability

Underlying data

University of Sheffield ORDA: Orphan Drugs - Dataset 1: Twitter issue-networks as excluded publics. https://doi.org/10.15131/shef.data.16447326.v1. (Hanchard (2021b))

This project contains the following underlying data:

- Issue-networks as excluded publics - Edges.csv (comprises all social network analysis edges (retweets/mentions). This encompasses detail on number of times (designated as weight) that a tweet is mentioned, liked, commented on, and/or retweeted. It uses unique ID to designate both sources (the originator of a tweet) and targets (those interacting with a source's tweet))
- Issue-networks as excluded publics - Nodes.csv (comprises all social network analysis nodes. This includes detail in the node name (label), i.e., Twitter user (or pseudonym), a unique ID, the number of tweets sent and mentions received, in/out-degree, closeness, and centrality measures. And modularity class (group/cluster))

Extended data

This project contains the following extended data:

- Issue-networks as excluded publics - ReadMe - About the dataset.docx

Acknowledgements

Thanks go to: the Twitter participants who kindly provided consent for use of their personal data; Dr. Warren Pearce for early discussion on the use of DMI-TCAT and Gephi; Dr. Stefania Vicari and four anonymous ethics review committee members at the University of Sheffield Research Ethics Committee for incisive advice and feedback on the research ethics; to my close colleagues Dr. Jin Ding and Dr. Eva Hilberg for constructive feedback on the narrative of an early draft; and to Prof. Paul Martin too, both for constructive comments and helpful feedback, and for allowing me the time and space to write the paper. Also, to the Facebook Gephi community (https://www.facebook.com/groups/gephi) for expert technical advice, tips, and support.

References

Bailey J: **NHL players, local businesses help Kootenay man raise funds and awareness for rare genetic disease.** *Trail Times.* 2021.
Reference Source

Bauer L: **Supporting Rare Disease Drug Development: CDER's Rare Diseases Program: 2017 Roadmap for Engaging with the Center for Drug Evaluation and Research**. 2017.
Reference Source

Blondel V, Guillaume, JL, Lambiotte R, *et al.*: **Fast unfolding of communities in large networks.** *J Stat Mech.* 2008; **P10008**(10).
Publisher Full Text

Bloor D: **Durkheim and Mauss revisited: Classification and the sociology of knowledge.** *Stud Hist Philos Sci: Part A.* 1982; **13**(4): 267-297.
Reference Source

BrainStorm: **BrainStorm Announces Topline Results from NurOwn® Phase 3 ALS Study**. 2020.
Reference Source

Bruns A: **How long is a Tweet? Mapping dynamic conversation networks on Twitter using GAWK and Gephi.** *Information Communication and Society.* 2012; **15**(9): 1323-1351.
Publisher Full Text

Burgess J, Matamoros-Fernández A: **Mapping sociocultural controversies across digital media platforms: one week of #gamergate on Twitter, YouTube, and Tumblr.** *Communication Research and Practice.* 2016; **2**(1): 79-96.
Publisher Full Text

Change.org: **European Commission: Acceso temprano a tratamiento para la ELA**. 2021.
Reference Source

Denton N, Molloy M, Charleston S, *et al.*: **Data silos are undermining drug development and failing rare disease patients.** *Orphanet J Rare Dis.* 2021; **16**(1): 161.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

de Saille S: **Innovating innovation policy: the emergence of 'Responsible Research and Innovation.** *J Responsible Innov.* 2015; **2**(2): 152–168.
Publisher Full Text

de Saille S, Martin P: **Monstrous regiment versus Monsters Inc.: Competing imaginaries of science and social order in responsible (research and) innovation**. In: Nerlich, B., Hartley, S. Raman, S., & Smith, A. (Eds.), *Science and the politics of openness: Here be monsters*. Manchester University Press: Manchester. 2018; 148–167.
Reference Source

EMA: **EMA/313148/2020: Meeting summary-PCWP/HCPWP joint meeting (Report) Amsterdam: European Medicines Agency.** 2020.
Reference Source

English Standard Version Bible. ESV Online. 2001.

FDA: **Right to Try. Learn About Expanded Access and Other Treatment Options**. 2021.
Reference Source

Feemster LC, Lyons PG, Chatterjee RS, *et al.*: **Summary for Clinicians: Lymphangioleiomyomatosis Diagnosis and Management Clinical Practice Guideline.** *Ann Am Thorac Soc.* 2017; **14**(7): 1073-1075.
PubMed Abstract | **Free Full Text**

Felt M: **Social media and the social sciences: How researchers employ Big Data analytics.** *Big Data Soc.* 2016; **3**(1): 205395171664582.
Publisher Full Text

Gerlitz C, Rieder B: **Mining One Percent of Twitter: Collections, Baselines, Sampling.** *M/C Journal.* 2013; **16**(2): np.
Publisher Full Text

Groshek J, de Mees V, Eschmann R: **Modeling influence and community in social media data using the digital methods initiative-twitter capture and analysis toolkit (DMI-TCAT) and Gephi.** *MethodsX.* 2020; **7**: 101164.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Groshek J, Tandoc E: **The affordance effect: Gatekeeping and (non)reciprocal journalism on Twitter.** *Comput Hum Behav.* 2017; **66**(1): 201-210.
Publisher Full Text

Guest G, MacQueen K, Namey E: **Planning and Preparing the Analysis.** In: Guest, G., MacQueen, K., & Namey, E. (Eds.) *Applied Thematic Analysis.* Sage: London, 2014; 21-38.
Reference Source

Hanchard M: **The construction of rare disease discourse on YouTube: highlighting a disparity between policy rhetoric and patient practices around public engagement [version 1; peer review: 1 approved with reservations].** *Wellcome Open Res.* 2021a; **6**(361).
Publisher Full Text

Hanchard M: **Orphan Drugs - Dataset 1: Twitter issue-networks as excluded publics.** [Dataset] ORDA: Sheffield. 2021b.
http://www.doi.org/10.15131/shef.data.16447326.v1

Hansen DL, Shneiderman B, Smith MA, *et al.*: **Social network analysis: Measuring, mapping, and modeling collections of connections.** In: (eds.) Hansen, D., Shneiderman, Smith, M., and Himelboim, I., *Analyzing Social Media Networks with NodeXL: Insights from a Connected World.* Morgan Kaufmann: Burlington, MA. Chapter 3. 2020.
Publisher Full Text

Himelboim I, Smith M, Rainie L, *et al.*: **Classifying Twitter Topic-Networks Using Social Network Analysis.** *Social Media + Society.* 2017; **3**(1): 1–13.
Publisher Full Text

HM Govt: **Genome UK: the future of healthcare [Report].** 2020.
Reference Source

HM Govt: **England Rare Diseases Action Plan 2022 [Report].** 2022.
Reference Source

Jacomy M, Venturini T, Heymann S, *et al.*: **ForceAtlas2, a continuous graph layout algorithm for handy network visualization designed for the Gephi software.** *PLoS One.* 2014; **9**(6): e98679.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Keller B, Labrique A, Kriti J, *et al.*: **Mind the Gap: Social Media Engagement by Public Health Researchers.** *J Med Internet Res.* 2014; **16**(1): e8.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Landherr A, Friedl B, Heidemann J: **A Critical Review of Centrality Measures in Social Networks.** *Bus Inf Syst Eng.* 2010; **2**(6): 371–385.
Publisher Full Text

Marres N: **Why Map Issues? On Controversy Analysis as a Digital Method.** *Sci Technol Human Values.* 2015; **40**(5): 655–686.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Marres N, Moats D: **Mapping Controversies with Social Media: The Case for Symmetry.** *Social Media + Society.* 2015; **1**(2): 1–17.
Publisher Full Text

Marres N, Rogers R: **Recipe for tracing the fate of issues and their publics on the Web**. In: Latour, B., & Weibel, P. (Eds.), *Making Things Public: Atmospheres of Democracy*. MIT Press: Cambridge, MA. 2005; 922–935.
Reference Source

McKee K, Richardson K: **Improving access and awareness of rare disease trials through patient and registries**. World Orphan Drug Congress USA 2021. [Presentation]. 2021.
Reference Source

McMullan J, Crowe A, Downes K, *et al.*: **Carer reported experiences: Supporting someone with a rare disease.** *Health Soc Care Community.* 2021; **30**(3): 1097–1108.
PubMed Abstract | **Publisher Full Text**

Mesko B, deBronkart D: **Patient Design: The Importance of Including Patients in Designing Health Care.** *J Med Internet Res.* 2022; **24**(8): e39178.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Münch F, Thies B, Puschmann C, *et al.*: **Walking Through Twitter: Sampling a Language-Based Follow Network of Influential Twitter Accounts.** *Social Media + Society.* 2021; **7**(1): 1–17.
Publisher Full Text

Newman M: **Modularity and community structure in networks.** *Proc Natl Acad Sci U S A.* 2006; **103**(23): 8577–8696.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Omena J, Rabello E, Mintz A: **Digital Methods for Hashtag Engagement Research.** *Social Media + Society.* 2020; **6**(3): 1–18.
Publisher Full Text

Rare Disease Day: **Events**. [Webpage]. 2021.
Reference Source

Rogers R: **Digital Methods**. MIT Press: Cambridge, MA. 2013.
Publisher Full Text

Valente M, Cesuroglu T, Labrie N, *et al.*: ***When Are We Going to Hold Orthorexia to the Same Standard as Anorexia and Bulimia?* Exploring the Medicalization Process of Orthorexia Nervosa on Twitter.** *Health Commun.* 2022; **37**(7): 872–879.
PubMed Abstract | **Publisher Full Text**

Venturini T, Jacomy M, Jensen P: **What do we see when we look at networks: Visual network analysis, relational ambiguity, and force-directed layouts.** *Big Data Soc.* 2021; **8**(1): 1–16.
Publisher Full Text

Vicari S, Cappai F: **Health activism and the logic of connective action. A case study of rare disease patient organisations.** *Inf Commun Soc.* 2016; **19**(11): 1653–1671.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Voss J: **Re-making the modern constitution: The case for an observatory on public engagement practices**. In: Simon, D., Kuhlmann, S., Stamm, J., & Canzler, W. (eds.). *Handbook on Science and Public Policy*. Edward Elgar: Cheltenham. 2019; 67–91.
Publisher Full Text

Walter S, Lörcher I, Brüggemann M: **Scientific networks on Twitter: Analyzing scientists' interactions in the climate change debate.** *Public Underst Sci.* 2019; **28**(6): 696–712.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Wynne B: **Public Participation in Science and Technology: Performing and Obscuring a Political-conceptual Category Mistake.** *East Asian Sci Technol Soc.* 2007; **1**(1): 99–110.
Publisher Full Text

Yáñez-Muñoz R: **10 Years of Rare Disease Day.** *Gene Ther.* 2017; **24**(2): 67.
PubMed Abstract | **Publisher Full Text**