RESEARCH ARTICLE

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

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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
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 retweet 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/legitimate 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 anthropographics 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 visualisation 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 Marrés 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 ‘#rarediseaseaday’ 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, 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.**
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 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.

<table>
<thead>
<tr>
<th>User</th>
<th>Tweets</th>
<th>Followers</th>
<th>Mentions</th>
<th>In/out degree</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>MiguelPera</td>
<td>369</td>
<td>371</td>
<td>0</td>
<td>0 / 81</td>
<td>Patient Group</td>
</tr>
<tr>
<td>AlsPortugal</td>
<td>288</td>
<td>547</td>
<td>0</td>
<td>0 / 69</td>
<td>Patient Group</td>
</tr>
<tr>
<td>MatildeJA7421998</td>
<td>270</td>
<td>199</td>
<td>35</td>
<td>21 / 50</td>
<td>Patient</td>
</tr>
<tr>
<td>Noinvisibles</td>
<td>268</td>
<td>48,948</td>
<td>851</td>
<td>682 / 57</td>
<td>Organisation/Platform</td>
</tr>
<tr>
<td>AlteringALS</td>
<td>255</td>
<td>861</td>
<td>5</td>
<td>5 / 51</td>
<td>Patient</td>
</tr>
<tr>
<td>MA89271790</td>
<td>239</td>
<td>126</td>
<td>56</td>
<td>27 / 34</td>
<td>Retweet bot*</td>
</tr>
<tr>
<td>AndreiaValles</td>
<td>226</td>
<td>80</td>
<td>14</td>
<td>14 / 49</td>
<td>Patient</td>
</tr>
<tr>
<td>GuidoGidon</td>
<td>226</td>
<td>72</td>
<td>0</td>
<td>0 / 40</td>
<td>Patient</td>
</tr>
<tr>
<td>RareDiseases</td>
<td>215</td>
<td>35,249</td>
<td>916</td>
<td>720 / 167</td>
<td>NORD</td>
</tr>
<tr>
<td>JulesDeol547981</td>
<td>215</td>
<td>132</td>
<td>0</td>
<td>0 / 45</td>
<td>Patient</td>
</tr>
<tr>
<td>Mirabella82676571</td>
<td>213</td>
<td>93</td>
<td>53</td>
<td>21 / 33</td>
<td>Patient</td>
</tr>
<tr>
<td>Eliana1678422</td>
<td>209</td>
<td>30</td>
<td>0</td>
<td>0 / 45</td>
<td>Patient</td>
</tr>
<tr>
<td>smardiac</td>
<td>195</td>
<td>358</td>
<td>41</td>
<td>12 / 129</td>
<td>Charity</td>
</tr>
<tr>
<td>delphiniumpearl</td>
<td>171</td>
<td>147</td>
<td>2</td>
<td>2 / 87</td>
<td>Retweet bot*</td>
</tr>
<tr>
<td>Mariana5457481</td>
<td>169</td>
<td>110</td>
<td>38</td>
<td>18 / 49</td>
<td>Patient</td>
</tr>
</tbody>
</table>
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 possibilitiess (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 with discussion of various rare diseases, not just one disease, shared orientation around religiosity. Their tweets also intersected a diffusion of power across various users albeit centred by a content aggregation site) were equally influential, illustrating

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 sugismunposted 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_ong (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 (skryiakideseu), and a pharmaceutical company specializing in neurodegenerative disorders (amylysfarma). 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.
Table 2. Fifteen most mentioned users.

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

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).
Together, these findings highlight a diffusion of power in issue-networks around mentions that differs from vocal-ity, 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 *possibilities* 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 reapropriated
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 #RareDiseaseDay2021 #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-

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**Figure 11.** Three issue-networks (ALS, LAM, and AD) on mentions.
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. Inspirational 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 requeoting 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?” [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, the specificity of LAM as a disease was far more direct. For example, one delphiniumpearl retweet broadcast the American Thoracic Society (ATSfellow) to a wider audience:

RT @ATSfellows: ATS summary of LAM for clinicians Link: https://t.co/1KAMoYp6x 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/ZbK3AhwiwD 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 caus- ing 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/ICUCharts/status/1090957169611235330)

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, smardiac continued to be highly vocal, tweeting in for example 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/status/1266381373413367666)

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 (or pseudonym), a unique ID, the number of tweets sent and mentions received, in/out-degree, closeness, and centrality measures. 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

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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