Title

The COVID-19 Global Rheumatology Alliance: Evaluating the rapid design and implementation of an international registry against best practice

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ABSTRACT

Background As the coronavirus disease (COVID-19) pandemic developed there was a paucity of data relevant to people living with rheumatic disease. This led to the development of a global, online registry to meet these information needs.

Objectives This manuscript provides a detailed description of the COVID-19 Global Rheumatology Alliance (GRA) registry development, governance structure, and data collection, and insights into new ways of rapidly establishing global research collaborations to meet urgent research needs.

Methods We use previously published recommendations for best practices for registry implementation and describe the development of the GRA registry in terms of these steps. We identify how and why these steps were adapted or modified. In phase 1 of registry development, the purpose of the registry and key stakeholders were identified on online platforms, Twitter and Slack. Phase 2 consisted of protocol and data collection form development, team building, and the implementation of governance and policies.

Results All key steps of the registry development best practices framework were met, though with the need for adaptation in some areas. Outputs of the registry, two months after initial conception, are also described.

Conclusions The GRA registry will provide highly useful, timely data to inform clinical care and identify further research priorities for people with rheumatic disease with COVID-19. The formation of an international team, easily able to function in online environments and resulting in rapid deployment of a registry is a model that can be adapted for other disease states and future global collaborations.

KEYWORDS: COVID-19, coronavirus, registries, rheumatic disease

KEY MESSAGES:

- The COVID-19 Global Rheumatology Alliance rapidly facilitated a global registry that collects de-identified data on people with rheumatic disease who develop COVID-19 via online platforms, in parallel with a European registry using the same data collection methods.
- Registry development adhered to all best-practice steps but concurrently or in a different order.
- Online platforms can enable rapid research collaboration to address urgent health crises.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has caused excess morbidity and mortality and disrupted work and social interactions [1]. People with rheumatic disease (RD) may have additional burdens due to potentially increased risk of infection with the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the unknown impact of RD or its treatment on the course of COVID-19 [2]. There is an urgent need for data about the impact of COVID-19 on people with RD. Previous viral epidemics have not had the same geographical or numerical impact, been sufficiently novel, or had hypothesized increased risk for people with RD to galvanise global research efforts focusing on this population. The unprecedented impact of COVID-19 necessitates immediate action.

The development of a registry is an appropriate approach to collect structured data about outcomes for people with RD in an epidemic. Traditional registry development follows two phases [3]: Phase one articulates a purpose, determines if a registry is appropriate to achieve the purpose, identifies stakeholders, and determines feasibility. Phase two includes building a team, establishing governance, defining scope and rigor, defining a dataset, developing a protocol, and a project plan. These steps may take years [4-6]. Traditional approaches would be unlikely to provide information in the time frames demanded by the COVID-19 pandemic, where the documented global mortality exceeded 150,000 individuals in less than six weeks [7].

The online presence of healthcare professionals (HCPs) and researchers provides a unique opportunity for collaboration. A global research team with established virtual professional networks in social media can work outside the usual institutional and geographic boundaries. On 11th March 2020, discussion began on Twitter amongst the rheumatology community about the possibility of a global rheumatology COVID-19 registry. On 24th March the COVID-19 Global Rheumatology Alliance (GRA) provider-entered registry was launched [8].

This manuscript describes the rapid implementation of a global rheumatology provider-entered registry to urgently provide information and knowledge to people with RD and their HCPs to achieve the best health outcomes during the COVID-19 pandemic. We provide a detailed description of the GRA Registry development, governance structure and data collection, and insights into the rapid establishment of a global research collaboration. We will evaluate the GRA Registry development against recommendations for best practices – and reflect what can be learned about developing registries via online collaboration during an emergent health crisis.

METHODS

Phase 1 of the development of the GRA registry occurred within one week via online platforms. Phase 2 consisted of overlapping/contemporaneous steps.

Phase 1: Planning the registry

The need for, and purpose of, the registry must first be clearly articulated [3]. Stakeholders should be identified, and they should gain a clear understanding of what data are being collected, and how it will be used. This depends on clarifying key questions that the registry seeks to answer, and whether those questions can be addressed via a registry.

Twitter

On 11th March 2020, a senior rheumatologist based in the USA retweeted an update on the SECURE-IBD registry [9] and asked: “Are we doing this in RHEUM yet?” [10]. The responses included: 1. acknowledgment that there were no data on COVID-19 disease outcomes in people with RD (indicating an established need); 2. proposed use of a manual entry, de-identified RedCap Survey for data entry; 3. identified the need for ethical approval; and 4. identified a survey already under development by a rheumatologist.

Slack

To facilitate collaboration, a Slack workspace was established on the 12th March 2020. Slack [11] is a proprietary business communication platform with “channels” organised by topic or for groups of people, and allows direct messaging. In addition, Slack permits

document sharing and integration with a number of cloud sharing platforms. Slack enabled more detailed discussions about registry feasibility and key questions that a registry could and could not answer. The discussions also identified the limitations of a registry when data are collected with a de-identified, provider-entered survey, such as selection bias, and delays in data entry.

Due to the urgent need for information, feasibility was confirmed for the short term only; the survey could be developed using “in-kind” personnel and hosted at an academic institution at no cost. It was identified that the General Data Protection Regulations of the European Union, which have specific requirements for data storage and management, necessitated a separate provider survey managed via the European League Against Rheumatism (EULAR).

Phase 2, Part 1: Defining the protocol and dataset

In the Gliklich et al framework [3], defining the dataset and developing a protocol occurs last. The GRA registry protocol and dataset were developed concurrently with the steps of Phase 1, as was the initial team building.

Protocol and dataset

Over the next 24-48 hours, the GRA was formed and academic rheumatologists began drafting a study protocol. The data elements for the registry survey were derived from 1. a RedCap survey drafted by a US academic rheumatologist; 2. data elements from the SECURE-IBD registry; and 3. WHO COVID-19 data elements [12]. The preliminary case report form was posted on Slack with approximately 20 people giving feedback. An experienced data management and analytics team of ten people at the University of California, San Francisco (UCSF) refined survey questions based on the feedback and configured the branch logic. Drafts of the RedCap survey were posted to Slack for final review and revisions. Beta versions of the RedCap survey were piloted via email by GRA members.

Ethics

Since the Global RedCap survey was hosted on secure servers at UCSF, an expedited IRB process was undertaken there, with approval on 16th March, 2020. The intent was for UCSF to be the central IRB for all US sites.

EULAR COVID-19 registry

The final RedCap survey was provided to EULAR so an identical European registry could be established. The EULAR registry is stored at The University of Manchester (data processor), with EULAR being the data controller. The EULAR COVID-19 database has a separate steering group [13]. The shared goal was to combine data for analysis from the two parallel registries.

Phase 2, Part 2: Building the team

In building the team that manages the registry, the following should be considered, and roles assigned to key members: project management, subject matter expertise, data collection and management, and legal matters [3]. When the development timeframe is compressed, a clear delineation of these roles becomes even more important.

Steering Committee

The Steering Committee formed from the initial responders on Twitter. The Committee performs project management, subject matter expertise roles, and addresses legal matters. The Chair and Vice-Chair had designed the protocol and initiated the IRB process (PR, JY). Two rheumatologists with expertise in social media and technology became leads for technology (PS) and external relationship and media communication (SB). A budget was formed to account for fiscal year 2020 and plan for fiscal year 2021 (SB). Two academic rheumatologists were appointed leads for coordinating knowledge synthesis and dissemination (RG, ZW). The Steering Committee also includes patient members (ES, WC), and a physician to specifically support the separate project of a Patient Experience Survey (JH). A trainee-level member joined to manage regional leads and co-ordinate external communication (JL). Two members are also formal liaisons with

the American College of Rheumatology (SB, ZW). A European member was included to represent the EULAR-based registry (PMM).

Data analytics

The GRA Vice-Chair was able to leverage an existing, funded data analytics team at UCSF to build the RedCap survey and manage the output of the provider registry. This team included epidemiologists and biostatisticians with extensive experience in the analysis and management of registry data [14]. This team resolved data entry issues for investigators, validated and cleaned incoming data, and performed analyses.

Collaborators

Via Slack volunteers became regional leads, responsible for coordinating local institutions to contribute to the provider registry. Slack members emailed national or international professional and patient organisations to seek the endorsement of the registry. At the EULAR level, partnerships were established with national societies that already had local registries collecting information about COVID-19 in RD.

Phase 2, Part 3: Establishing governance and policies

The GRA Steering Committee developed policies for data requests and governance over outputs from the GRA registry data. Internal projects were defined as projects originating from the Steering Committee and external projects defined as all projects from outside the Steering Committee, which would require application, approval, and monitoring, by a designated Data and Sharing Committee.

RESULTS

We outline how the registry met, or otherwise, the steps in the Gliklich framework (Table 1), summarise the timeline, and describe the outputs after two months.

Phase 1: Planning the registry

Within hours of the initial tweet, the purpose and need of a rheumatology-specific registry were established. Within a week, there was a clear articulation of the purpose of the

registry, which is to collect data to describe the general characteristics of COVID-19 in people with RD, address whether background immunosuppressive medications put individuals with RD at an increased or decreased risk for severe SARS-CoV-2 infection, and to gather information to guide treatment decisions.

Phase 2, Part 1: Defining the protocol and dataset

Practical considerations identified in Slack channel discussions of the draft data collection form were the need to collect both detailed and accurate information, and have a short survey for full completion by clinicians. It took five days from initial tweet to IRB approval (17th March 2020), 13 days to launch of the global registry (24th March 2020) and 16 days to launch of the EULAR registry (27th March 2020).

Phase 2, Part 2: Building the team

The development of the core team, the Steering Committee, occurred alongside the initial tweets and emails. Committee members were able to leverage their interests and experiences to fulfill necessary roles. By 5th May 2020, over 300 international organisations endorsed the GRA provider registry (Figure 1) and over thirty sites had obtained ethical approval for data submission.

Phase 2, Part 3: Establishing governance and policies

Gliklich et al recommend the development of policies before protocol and plans for outputs. GRA policies were developed as the need became apparent: initial policies include those on authorship, data sharing, and internal and external projects, all developed under a truncated timeline.

Outputs

Clinicians who provide care to patients with RD may enter the cases of patients with confirmed or suspected COVID-19 directly into the RedCap survey form (supplemental material) via the GRA website. Key data collected includes demographics, rheumatic disease status (type, activity, and medications), and COVID-19 disease course and treatment. While patients cannot enter their own data, they are encouraged to

participate in the Patient Experience Survey which will also collect data about less severe COVID-19 cases (19). Since the registry allows case entry before outcomes (recovery versus death) are known, the data analytics team keeps track of, and contacts physicians to enter data about case resolution.

The GRA tweeted interim data on 47 patients on 30th March 2020. The first publication, of descriptive statistics for 110 patients, appeared electronically on 16th April 2020 [15]. The first multivariable analysis of 600 cases from the two combined provider registries was accepted for publication on 11th May [16].

DISCUSSION

We described our rapid, online registry development against the best practice framework of Gliklich et al. All steps were met, but conducted concurrently or in a different order. We demonstrate online platforms can facilitate rapid registry development, and so provide a blueprint for future rapid registry implementation.

The GRA registry was inspired by the global SECURE-IBD registry, which aims to assess COVID-19 outcomes for people with inflammatory bowel disease, via reporting of de-identified patient data [17]. Walkey et al have also described the implementation of a similar online registry for COVID-19 critical care patient data [18]. There are similarities between the Viral Infection and Respiratory Illness Universal Study (VIRUS) registry and the GRA registry: both were conceptualized on Twitter, rapidly developed case report forms for data collection, and have required real-time policies on governance and data sharing. The GRA has also applied many of these lessons to a patient experience survey [19]. These registries illustrate the international reach and impact of virtual professional networks online, with the ability to build a team, infrastructure and link with stakeholders in days.

Challenges and future directions

The GRA registry development was not without challenges. Although we obtained central IRB approval from a US site, many participants requested confirmatory ethical approval

and data use agreements from their individual institutions. Investigators from other countries had to navigate varying IRB procedures, with Europe also requiring a separate, parallel registry. While Slack enabled the management of a large number of volunteers, coordination of projects and enabling equitable access of volunteers to project work remains challenging. The Steering Committee addressed issues of representation and equity, including authorship and leadership on registry-related projects, by drafting policies in real-time.

While the GRA registry will provide highly useful insights, this approach has limitations. The GRA registry has potential for selection bias (e.g. more severe cases) which may limit generalizability. Furthermore, the GRA data cannot be used to estimate incidence rates of infection among individuals with RD, or to compare those with and without COVID-19. There is also wide geographic variation in reporting, driven by the incidence of COVID-19 in the general population, as well as barriers to reporting by clinicians. These points will be accommodated in analysis and acknowledged in dissemination of data.

The GRA registry feasibility was only confirmed for the short term. The American College of Rheumatology has provided a mechanism for the management of funding while maintaining the independence of the GRA. This will allow the procurement of funds for sustainable project management and data analytics. Ongoing engagement with stakeholders including professional organisations and expanding data entry to less well-represented areas are priorities. Establishing teams to undertake data analysis and dissemination is ongoing. Future projects include collaborations and potential linkage with COVID-19 registries in other diseases, including IBD, as well as with general RD registries.

Limitations

This was a qualitative description of our registry processes and implementation. We used a published registry development framework and relied on previously published

descriptions of similar registries. However, there is no standardized guideline for registry implementation.

Conclusions

The rheumatology community identified a need to build a global, online registry to collect data on patients with rheumatic disease with COVID-19 infections. We reviewed the implementation of this registry over the course of two months based on a best practice model for registry development. We highlighted the adaptations as well as challenges to our approach. Current priorities include establishing a sustainable financial model and data analysis and dissemination via the peer-reviewed literature.

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SB reports no competing interests related to this work. He reports non-branded marketing campaigns for Novartis (<$10,000).

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ES reports no disclosures.

PS reports no competing interests related to this work. He reports honorarium for doing social media for American College of Rheumatology journals (<$10,000).

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Table 1. Steps in registry development per Gliklich et al and modification for the GRA Registry

Step in developing a registry	**Completion by the GRA Registry**
Articulate the purpose of the registry	Done on Twitter, within first 24-48 hours
Determine if a registry is the appropriate means to achieve the purpose	Done on Twitter, within first 24-48 hours
Identify key stakeholders	Done on Twitter, within first 24-48 hours; an iterative process
Determine the feasibility of a registry	Done on Twitter, within first 24-48 hours
Build a registry team	Done on Twitter and Slack
Establish a governance and oversight plan	Paralleled other steps of registry development
Define scope and rigor needed	Done on Slack; feedback from GRA members
Define the dataset, patient outcomes, and target population	Done on Slack; feedback from GRA members
Develop a study plan or protocol	Done via email, within the first week
Develop a project plan	Done on Slack; iterative process

Figure 1. World map with the number of supporting organizations by country