

REPORT

The CORRONA database

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The Consortium of Rheumatology Researchers of North America (CORRONA) was founded by a group of academic rheumatologists. CORRONA was designed to fill a void in North America as, at the time of its founding, there was no database independent of the pharmaceutical industry that collected data in the clinic from both rheumatologists and patients. CORRONA began collecting data in 2002.

There was also a perceived need to develop a database which collected clinical information from all patients with rheumatoid arthritis in a practice. With the introduction of expensive new therapeutic agents, it was apparent that longitudinal, long term, “real world” data would serve the rheumatology community well. There was also the perception that busy physicians would welcome a system that enabled them to treat individuals with chronic diseases associated with complex comorbidities in a smart and efficient manner while reliably tracking standard outcomes, laboratory and imaging data, as well as toxicities. The new agents have the potential for great individual and societal good, as well as the potential for frightening toxicities. It was apparent that reliance on voluntary reporting from post-marketing surveillance to the Food and Drug Administration (FDA), and various long term phase IV studies would not be adequate to inform fully rheumatologists and patients about outcomes in this evolving clinical marketplace.

DESCRIPTION OF THE DATABASE

At the time of this writing, June 2005, the CORRONA database has 8755 patients with rheumatoid arthritis, 955 patients with psoriatic arthritis, and approximately 1000 patients with a primary diagnosis of either osteoarthritis or osteoporosis. There are 83 sites scattered in 33 states in the USA (fig 1), and a total of 200 rheumatologists now participate. Patients with rheumatoid arthritis or psoriatic arthritis are enrolled at the time of a routine visit at a site. They are then followed as often as every three months for rheumatoid arthritis, and every six months for psoriatic arthritis, osteoarthritis, and osteoporosis. At the time of this writing the database consists of more than 30 000 total visits, with a mean duration of follow up of 1.27 years. The mean time between follow up visits for patients in the database is 5.7 months, with a total of 7368 patient years for patients with rheumatoid arthritis.

ACADEMIC REPORTS

For a longitudinal database to be of value, it must mature to the point that data are meaningful. That is, the data have to have intrinsic recognisable value. This “tipping point” occurs when there are enough patients in the database for a sufficient length of time to enrich the data to the point of relevance for the clinical community. Getting to the point of meaningful data is obviously a process which does not occur overnight. At the end of our third year of existence, we can now say with some confidence that CORRONA is at that point. Earlier observations from the database published in abstract form^{1–9} have recently been followed by full-length

reports¹⁰ and several other data submissions to both the annual meeting of the European League Against Rheumatism (EULAR)^{11–15} as well as the annual meeting of the American College of Rheumatology.^{16–27} It is apparent that the data have now been enriched and have matured to the point of clinical relevance. It is appropriate then that a flurry of reports begin to emerge at this time.

CONTEXT

It is perhaps somewhat surprising that similar efforts have not been previously initiated. Others have advocated for the collection of data in the clinic using standardised forms for many years.^{28–29} In addition, standardised longitudinal databases have emerged in Sweden³⁰ and the UK,³¹ and these have already made substantial contributions. The Swedish data are derived from a national healthcare registry, so that the data come from a pre-existing computer system established by the national healthcare delivery system of Sweden. The system in the UK is voluntary and not universal.

It was not clear if busy rheumatologists in the USA would voluntarily participate in data collection in the clinic. These physicians were felt to be too “flat-out busy” to voluntarily assume the added task of collecting data on forms. Thus, any system which was based on the assumption that physicians would collect data had to have considerable built-in advantages, or incentives, for the clinician if it was going to realistically be capable of moving busy practitioners to change the way they did things. There were, however, several historical themes which have favourably affected the adoption of the process. Some of these factors were new and were not previously available to have favourably influenced the widespread adoption of data collection. We will briefly summarise these themes and see how they influenced the climate at the time in which CORRONA was founded in the USA.

(1) Integration of IT in clinical practice

The electronic revolution of data collection and management in the late 1990s and early part of the first decade of the new millennium changed the way in which we all viewed the collection of information. Physicians manage multiple complex issues including disease states, drugs with toxicities, and human beings with all their complexities. The number of variables associated with effectively managing these disparate data elements was and is large indeed. It makes a great deal of sense to have computer help in this complex process. Fortunately, clinicians who are considering adopting the process now have established models outside our discipline for information management, as most are familiar with the advantages of computers by now.

It is in fact unimaginable that a group of professionals with years of postgraduate training would not already rely on

Abbreviations: ACR, American College of Rheumatology; CORRONA, Consortium of Rheumatology Researchers of North America; DAS, Disease Activity Score; MHAQ, Modified Health Assessment Questionnaire; SNP, single-nucleotide polymorphism

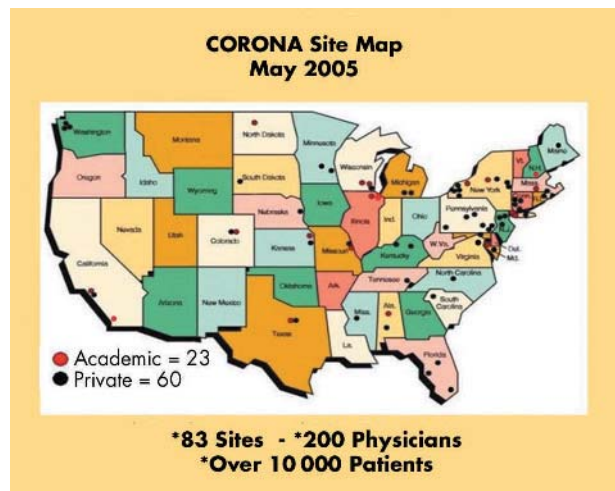


Figure 1 The Consortium of Rheumatology Researchers of North America (CORRONA) site map.

computer software to help them with the tasks of providing quality patient care while tracking the many complexities associated with management of disease outcomes, toxicities, and comorbidities. But, as has already been described, most practising rheumatologists in the USA completed their training at a time when computers and databases were not a part of their learning experience. These individuals became accustomed to making clinical decisions from their considerable fund of established medical judgement, or gestalt, which has been developed over the course of years of practice.

It was frankly difficult to recognise that there could have been "a better way" to take care of patients. Many physicians still cannot acknowledge that a better and more efficient pathway exists. Yet, it is readily apparent that the benefits would be great if an array of clinical information could be available to the treating rheumatologist at the time of every clinical encounter. This, combined with the increased awareness that even the most careful of physicians will inevitably omit a critical process when it has to be repeated hundreds, or thousands, of times makes the inclusion of an efficient and standardised patient interaction process crucial to avoid errors of omission.

(2) Billing Medicare

There is a need for documentation to assure that appropriate procedures have been performed to bill Medicare at a certain level of complexity. In the USA, certain elements of the clinical encounter such as two vital signs, a patient social history, as well as certain critical elements of the rheumatological examination such as a joint count, have to be present to defensibly bill Medicare (the US government sponsored system for payment of medical expenses for individuals over the age of 65) for what is called a "level IV" encounter. In the absence of a standardised system for assuring the presence of all of the necessary elements required to bill at this level, practice income suffers. The CORRONA forms provide the necessary documentation for this increased level of billing.

(3) Assurance of complete documentation

Busy clinicians need help in simply getting through their day. The complexities of patient care and appropriate documentation in the demanding political, economic, and social climate of the USA have combined to create increased stress for all physicians, and of course rheumatologists. A system which provides a focus for a clinical encounter is time neutral, while

providing patient care and documentation. A system that allows a busy rheumatologist to complete an encounter knowing that all of the critical elements of care have been addressed and documentation has been provided actually lessens stress while providing increased job satisfaction. This element of the data collection process should not be underestimated.

(4) Data analysis

Rheumatologists using CORRONA can access data on the web on all of their patients. By using their unique sign-in code, a participating clinician can view clinical, laboratory, and demographic data on the web. Customised analyses of individual patient data or patients grouped in a variety of ways (that is, by physician or provider, sex, age, drug prescribed, insurance type, laboratory abnormality, radiographic status, bone density status, etc.) are possible. This additional element of the database gives clinicians at each site an unprecedented analytic tool which actually goes beyond what is possible with an electronic database.

E-databases are able to provide descriptive data on many elements of disease and this feature is of course also found in the CORRONA database. However, e-databases are not able to create customised cross-analyses combining various data elements and presenting them in a customised graphic format. This additional element provided by the CORRONA database allows a level of sophisticated learning and appreciation of the nature of practice patterns which has no precedent. It can be used for business reasons: patients on drug A do better than patients not exposed to it; disability, hospitalisations, and orthopaedic procedures are reduced when we treat in this manner as documented in our database, etc. The information can therefore be used to defend prescribing patterns of expensive medications, maintaining therapeutic options with local payers. The information can also be used for academic investigations: does the combination of drug B used with methotrexate result in better outcomes than drug C used with methotrexate?

The data can be used to compare practice performance and outcome measures among several rheumatologists within the same practice to determine who is performing in a manner which actually results in the best practice and patient outcomes; several parameters could be used for this analysis including joint counts, Modified Health Assessment Questionnaire (MHAQ), frequency of corticosteroid injections, laboratory parameters, hospitalisations, orthopaedic procedures, development of comorbidities, etc.

(5) Physician reimbursement

Rheumatologists are paid by CORRONA for completing both baseline and follow up forms. This payment can represent a significant additional source of income at a time when other revenues are diminishing.

(6) Expanding opportunities for individual physicians to participate in research

Many clinicians feel only partially fulfilled with the process of seeing patients. Participation in CORRONA allows rheumatologists the opportunity to contribute to the greater good by participating in a national team effort, led by academicians within their own discipline and whom they respect, to learn more about the diseases which they treat. In addition, individual site participants have the opportunity to query the entire database annually by submitting queries to the Scientific Committee of CORRONA. These submissions are reviewed in a timely manner prior to the deadline for an abstract to the annual meeting of the American College of Rheumatology. They are numerically ranked by our scientific committee for quality and, if accepted, any member of the

network can use the services of the full-time statistical support staff of CORRONA to develop the data for a submission and manuscript.

All of these components of context favouring the adoption of a web based database are summarised in box 1.

GOVERNANCE

CORRONA is run by a board of directors of rheumatologists. Its governance is entirely independent of any outside industry influence. The board meets monthly in a tele-conference to discuss all issues of governance. Scientific policy is set by the Scientific Committee of six members which also determines the merits of abstract submissions and fellowship awards. An Executive Committee of five members develops policy recommendations which are then brought to a vote by the entire board membership at the time of the monthly meeting. A recruitment and follow up committee develops policy to help rheumatologists at sites and disseminate information to CORRONA patient participants about the accomplishments of the database and the organisation.

Board governance is based upon the principle of “one man, one vote”—that is, all opinions, votes and input count equally, without any single individual having more “pull” than anyone else. Board membership is for a finite period and new members rotate on while others rotate off. Physician members at CORRONA sites are eligible to be nominated for participation on the board. Individuals are chosen for a track record of academic leadership, contributions to the rheumatology community, and their potential for other organisational contributions because of demonstrated dedication to our goals, or unique skills which can contribute to the overall success of the organisation. At all times, a philosophy of inclusion in the process is adhered to by members of the board of directors. The governance of CORRONA does not wish to be perceived as an “old boys club” of privileged insiders. A member of the board is judged annually on tangible contributions, empowering so called “less visible” members to achieve positions of influence simply by hard work.

FUNDING

CORRONA derives operating funds from the pharmaceutical industry (Pharma). Pharma purchases the ability to access data from the CORRONA database. However, Pharma is not allowed to simply see or use raw data. Rather, Pharma purchases a number of hours of access quarterly to the CORRONA biostatistical team. Pharma submits a query for analysis of a particular question, or questions. In the next step, a member of the CORRONA Board of Directors sees the

Box 1: Historical and contextual reasons favouring widespread adoption of the CORRONA database

- (1) Information management
- (2) Documentation for billing
- (3) Stress reduction from knowing that all elements of an encounter have been efficiently covered
- (4) Ability to perform customised analyses on data from an individual site
- (5) Payment for baseline and follow up forms
- (6) Participation in the academic activities of the network

query(ies) and determines if it is appropriate—that is, is the database able to address the question, and is it an appropriate question? (Pharma is limited in asking questions which identify competitors by name, (see below).)

Assuming that the answers to these questions are affirmative, the CORRONA fulltime biostatistical staff begins a process of back and forth communication with the individuals in Pharma who have submitted the query. Analyses are then submitted and refined in an iterative process until all of the elements and components of the submission are answered in a satisfactory manner. It is from this Pharma support from multiple companies that CORRONA has derived working capital which may then be used to provide legal, biostatistical, infrastructure, and IT support, while paying rheumatologists for the forms.

Rules for utilisation of CORRONA data by Pharma

The pharmaceutical industry is limited in the use of CORRONA data as individually named patent-protected, competitor products cannot be identified in a promotional package or publication. Pharma can, however, compare their product with grouped products. That is, anti-tumour necrosis factor (anti-TNF) product “A” can compare results with products “B” and “C” grouped together, and not individually identified. Of course, all drugs can be compared with any generic agent, or group of agents in any manner. Generic agents can be grouped together with patent-protected drugs.

It was felt that the above policy protected CORRONA from the potential for use of its data in marketing battles between companies. Inevitably, it was felt that the credibility and stature of the database could be compromised if it were used primarily for marketing. In addition, before submitting any CORRONA derived report in the public domain, Pharma partners have to submit the report to the CORRONA biostatistical team for review.

Thus there are two quality control steps which Pharma must perform. Firstly, they receive answers to their submitted query from CORRONA’s own biostatistician, without seeing raw data. Secondly, before “going public” with a report, the data are again viewed by the CORRONA biostatistical team and checked for statistical veracity and accuracy. Finally, a member of the CORRONA board of directors may serve as an author on any submitted academic report or publication. (This process is not however mandatory, but generally felt to be a “plus” by industry.) In this manner CORRONA provides an additional quality oversight on the manner in which our data are reported to the rheumatology community.

FUTURE DIRECTIONS

Pharmacogenomics

CORRONA is in an ideal position to serve as the database from which pharmacogenomic data on the rheumatic diseases are derived. This is because the data are not limited by either a single drug, or even a single disease state. The CORRONA database has already begun to examine the association with certain single-nucleotide polymorphisms (SNPs) with disease outcomes from our database,^{16–18} and we anticipate greatly expanding these analyses with the addition of proteomic and biomarker measures.

One of the major developments in medicine in the past several years has been the conclusion of the identification of human genes from the Human Genome Project. Although many associations with rheumatic disease in general, and rheumatoid arthritis in particular, have been identified, science is not yet at the point where these analyses can support clinical decisions regarding treatment for patients. It is likely that thousands of patients will need to be studied to derive reliable conclusions. The marriage of a large longitudinal database like CORRONA with the ability to test

SNPs, proteomics, and biomarkers provides an unprecedented opportunity to derive these data as new and existing agents enter the clinic.

Quality management

Physicians in the USA are increasingly being made aware of the need for measurement of outcomes. An outcome which can be measured and assigned a numeric value can be tracked and has significant potential intrinsic value. Fortunately, validated outcome measures have already been developed and disseminated for widespread use in clinical practice. Thus “American College of Rheumatology (ACR) 20, 50, and 70” measures are routinely quoted by knowledgeable rheumatologists who are familiar with the published literature regarding the use of new agents. These outcomes can in fact be calculated from the CORRONA database as it contains all of the elements needed to calculate ACR scores. However, it is being increasingly recognised that ACR outcome measures are inadequate to represent change in individual patients. This is because these outcomes are binary systems in which an individual is assigned as achieving, or not achieving, the ACR outcome of interest. As such, they miss a gradation of responses which are in fact captured by the Disease Activity Score (DAS) 44 and DAS 28 outcome measures. Statistically, the ACR outcome is treated as a categorical variable, whereas the DAS is a continuous variable.

The above is offered in the way of background as it is likely that a validated outcome measure such as the DAS 28 will be used as a standardised, validated, continuous variable which can be used to track the clinical effectiveness of new and expensive interventions. Aside from the need to provide documentation for billing, and better patient related services, use of the DAS 28 from the elements of the CORRONA database will provide one of the key components of measurement (as performed by the physician, or physician extender, a continuous numeric value can be assigned) to track patient progress.

Some may say that it is not necessary and it is unlikely to be required that rheumatologists perform measurements like the DAS. They may be correct now, but in the brave new world of quality assessment and the assignment of monetary rewards for quality,³² it is apparent that objective, defensible measures of outcome (such as the DAS 28, the MHAQ (which also provides a numeric value which can be tracked), and the use of an electronic system which enables the clinician to track and monitor a variety of toxicities and comorbidities, receive prompts about needed elements such as tuberculosis skin testing, and testing and retesting of bone density will be necessary in order to fulfil the “QC” bill. Indeed, plans are now in place for Medicare to reward physicians with such quality measures by 2006.^{32, 33}

Sponsored studies

One of the original stated goals of CORRONA was to organise and sponsor our own studies of interventions for rheumatic diseases. There is presently no reliable mechanism to sponsor a study of an intervention of a new combination of existing agents to treat patients with either rheumatoid arthritis or psoriatic arthritis. The rheumatology community and our patients with rheumatic disease share clinical research choices which are understandably limited to those of the Pharma industry. This is because Pharma is the primary sponsor of clinical research in our discipline. Although funds for clinical research are theoretically available from the National Institutes of Health (NIH) and the Arthritis Foundation, in practice the former has not funded much in the way of clinical research and the latter does not have the funds for large scale investigations.

There is thus the need for an independent entity to develop the funding and infrastructure necessary to investigate the potential for combinations of new and existing agents to be used together. Other disciplines such as oncology has for some time been using protocols designed by experienced clinicians to determine which combination of drugs works best. It is possible that the new/biological agents combined with methotrexate are not an ideal combination if the therapeutic goal is to place patients in remission. If patent-protected drugs are to be prescribed and used together in rheumatology, with the goal of achieving a safe and lasting remission, a mechanism for funding investigations independent of Pharma will have to be developed. It is the hope of the board of directors that CORRONA can supply that mechanism.

Competing interests: none declared

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