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CRAJ SCR

The Journal of the Canadian Rheumatology Association

Focus on:

CRA Committee & Regional Association Reports

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- Reduction of signs and symptoms, induction and maintenance of clinical remission and induction of mucosal healing in pediatric patients with moderately to severely active UC who have had an inadequate response to conventional therapy (i.e., aminosalicylate and/or corticosteroid and/or an immunosuppressant)
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References: 1. Data on file, Janssen Inc.
2. REMICADE® Product Monograph, Janssen Inc., April 26, 2016.

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EDITORIAL

Little Data

By Philip A. Baer, MDCM, FRCPC, FACR

"When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts advanced to the stage of science." - Lord Kelvin

Everyone is talking about Big Data and its potential impact on medicine and business in general. Mining terabytes of data with supercomputers could lead to research breakthroughs, a cure for cancer, extended lifespans and personalized medicine. Closer to home, the investments physicians and governments have made in electronic medical records (EMRs) are partly premised on their eventual ability to provide a source of rich information. This could be combined with other existing databases to improve clinical care and allow every patient's clinical information to contribute to answering key unsolved questions in medicine.

The potential is staggering, as is the hype. This has been pointed out very recently in an editorial in the *Canadian Medical Association Journal (CMAJ)*[1]. Perhaps in the meantime, we can all try our hands at answering questions about our own practices using the data at hand. This would be very much in the spirit of practice self-audits, which are a key undertaking of the CRA, and are one of the best ways to obtain the newly required Royal College Section 3 credits for maintenance of certification.

Let me illustrate with a couple of examples from my own practice. I currently review all new referral requests personally. Most are accepted, some are rejected, and some result in requests for more information to determine their appropriateness and priority. What is the ideal ratio of these outcomes? No textbook will tell you. However, one can assess the possibilities with some simple analysis. I decided to count the number of spots available each week for new patients, and to compare this to the number of new referrals received per week. To obtain a reasonable sample, I collected these two data points over a four-week period not including any vacations, and then combined them into a single ratio of referrals received/referral spots available. As a thought experiment, consider a situation where 200 new referrals are received but only 10 referral appointments are available in a given period. The ratio would be 20. Stress would likely be high in such a practice. In this situation, I would suggest a strategy of accepting only those patients in greatest need of a rheumatologist (e.g., those with inflammatory arthritis, connective tissue diseases and vasculitis). Simple management suggestions and alternative referral possibilities could be provided to the primary care physicians of those patients not being accepted for consultation, along the lines of the rheumatology triage program operating in Calgary. On the other hand, if only 20 new referrals are received for 40 available spots, the ratio is 0.5. This could perhaps occur for someone newly in practice. In this situation, one might consider marketing their availability to the referring physician audience through a practice portal, providing CME lectures, or getting involved in a local medical association chapter. A ratio close to 1 would provide the least grief long-term, if achievable. It allows you to broaden your practice to whatever areas interest you outside of core inflammatory rheumatic diseases, including gout, osteoporosis, osteoarthritis and regional rheumatic disorders. Do you know your ratio? If you don't, are you making the most informed decisions possible about how you run your practice? The information is easily available and could be calculated on a running basis by your office staff.

Similarly, how do you decide on the ideal length of appointments for both new patients and follow-ups? Do you use tradition, guesswork or data? There is no average patient, but having 10 different lengths of appointments is also not practical. Say you allot 30 minutes for new referrals and 15 minutes for follow-ups. You may also know that more complex referrals actually end up taking 45 minutes. With a referral request/referral availability ratio of 20, almost all your referrals will be complex, and there is a mismatch between your appointment slots and the time actually required. With a ratio of 1, and knowing the prevalence of inflammatory diseases in Canada, you can be virtually certain that only 40-50% of your referrals will be so complex. Assuming simpler rheumatology problems can be handled in 20 minutes, especially with pre-office review of the patient's documentation, a 30-minute consult appointment slot now makes sense.

Follow-ups tend to be dominated by more complicated patients, as those with simpler conditions are best sent back to primary care for ongoing treatment. I like to run right

on time in my office, so any day I finish late provides an opportunity for reflection. I usually find that one particularly complex patient has required extra time. If I feel this will be an ongoing issue, I then assign that patient 30 minutes for their next follow-up. Much better to feel the office is moving along as scheduled next time, than to be running out of chairs in the waiting area. If the patient is doing better on the next visit, I can always use a few extra free minutes in the day, and they can return to a 15-minute spot thereafter. With the complexity of rheumatic diseases and their therapies, as well as an increasingly older follow-up population with multiple comorbidities, the number of patients permanently requiring longer follow-up spots will only grow. Empirically, I would also venture that requiring a longer follow-up appointment correlates with higher five-year mortality, but I am certainly not going to reveal that possibility to my patients in that situation. More research is required, both of the "little data" and "Big Data" varieties.

If you would like to contribute any examples of "little data" you have found useful in your practice, please send them to us at CRAJ for possible future publication.

1. Kirsten Patrick. Harnessing big data for health. CMAJ May 17, 2016 188:555; doi:10.1503/cmaj.160410

Philip A. Baer, MDCM, FRCPC, FACR
Editor-in-chief, CRAJ
Scarborough, Ontario

CRA EDITORIAL BOARD

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AWARDS, APPOINTMENTS, ACCOLADES

Dr. Claire Bombardier received the *Distinguished Clinician Scholar Award* from the American College of Rheumatology (ACR) at the 2016 annual meeting in November. The award is given to a rheumatologist who has made outstanding contributions in clinical medicine, clinical scholarship or education. Claire has demonstrated outstanding leadership in the areas of education, practice, research and policy. She has played a key role in mentoring women researchers who have become nationally and internationally recognized as leaders in their areas of expertise, including Sherine Gabriel, Gillian Hawker, Vivian Bykerk, Nancy Baxter, Dorcas Beaton, Rachelle Buchbinder, Aileen Davis, Jill Hayden, Andrea Furlan and Linda Li. Most recently, her work has focused on health system innovation to support rheumatologists, primary care providers and other advanced care clinicians.

At the American College of Rheumatology (ACR) 2016 meeting in Washington, the Lupus Foundation of America (LFA) awarded me the *Evelyn Hess Award* for Lupus Research. This award was established in 2005 and is given annually to a clinical or basic researcher whose body of work has significantly advanced understanding of the pathophysiology, etiology, epidemiology, diagnosis, or treatment of lupus. This award was created to recognize Dr. Hess' outstanding contributions to lupus research over the course of her long career. It is indeed a great honour to receive the *Evelyn Hess Award* from the Lupus Foundation of America. To be included among distinguished Lupus experts and to be acknowledged for doing something that I have enjoyed doing for the past 40 years is gratifying. I was particularly moved by the wonderful things said about me by the nominators for the award, David Isenberg and Ian Bruce.

Dr. Anna Oswald received the University of Alberta *Rutherford Award for Excellence in Undergraduate Teaching*, one of the university's most prestigious teaching awards. As one of only three awardees university-wide, she demonstrated a superior command of the content; an ability to instil vital interest in and enthusiasm for the subject; excellent planning and organization in course implementation; and the fostering of independent study, critical thinking and problem solving. She contributes to curriculum development and has served as a valuable resource for both students and colleagues. She promotes excellence in teaching by collaborating to generate a desire for continued learning. Her most substantial teaching activities included the complete redesign of the musculoskeletal pre-clerkship course and introduction of team-based learning to emphasize team learning, knowledge application and peer accountability.

Dr. Carter Thorne of Newmarket, Ontario, and a member of the Consultant Medical Staff at Southlake Regional Health Centre since 1980, was honoured with the designation of *Master* by the American College of Rheumatology (ACR) during the 2016 ACR/Association of Rheumatology Health Professionals (ARHP) Annual Meeting in Washington, D.C. Recognition as a Master is one of the highest honours that the ACR bestows on its distinguished members. Only 25 individuals received the designation, and Dr. Thorne was the only Canadian Master in 2016. "It's an honour to be recognized for my commitment to advancing the health of patients with rheumatic diseases," said Dr. Thorne "I am truly humbled to receive this designation and join the ranks of many distinguished rheumatologists." ACR Masters must be highly accomplished individuals and must be distinguished by the excellence and significance of his or her contributions to the science and art of rheumatology.

The *CRAJ* would also like to congratulate Dr. Kiem Oen and Dr. Alan Rosenberg for being designated *American College of Rheumatology (ACR) Masters* in 2015.

Training the Rheumatologists of Tomorrow (TROT): Addressing Human Resource Needs

By Diane Crawshaw, TROT Project Coordinator

In order to overcome the severe shortage of rheumatologists in Canada, we need more trainees at the postgraduate level; in 2012, we began a multiphase program funded by the CRA to help address this issue. Our aim was to produce and disseminate evidence-based messages about rheumatology for medical students and internal medicine residents, so that their future career choices would take into account first-hand knowledge about our subspecialty. We also wanted to form a pan-Canadian consortium of rheumatology programs to conduct and disseminate this work.

Having attained these goals over the last three years is a significant accomplishment for our national team led by Drs. Alfred Cividino and Kim Legault. During this time, the "Training the Rheumatologists of Tomorrow" (TROT) project developed a set of tools for educators, formed new partnerships across the country and disseminated findings at conferences, professional meetings, in a peer-reviewed journal and on the CRA website. We also mounted the *#MakeRheum* for Rheumatology campaign to encourage students to "make room" for an experience in rheumatology.

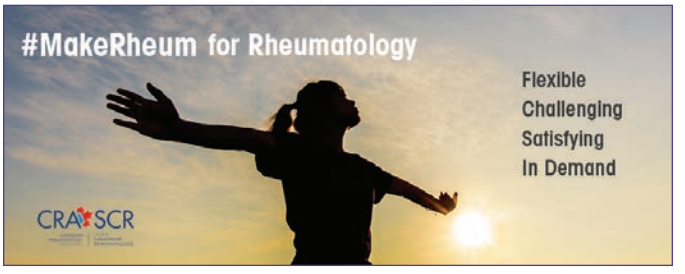
The resulting products are housed on the CRA website—please use them in your lectures and presentations. Print them, enlarge them and put them on your walls! In the spring of 2016, we sent a large package to each program that included laminated and mounted hero posters, the banner, and printouts of the slide deck of reasons to consider rheumatology (French versions were sent to our francophone programs). T-shirts were also distributed. Dr. Shirley Tse at the University of Toronto went one step further and had shirts printed for the whole group! So have fun with the materials and encourage your students to *#MakeRheum* for Rheumatology!

Most recently, with help from one of our rheumatology trainees, Caroline Barry from Dalhousie, a Facebook page (*https://www.facebook.com/MakeRheum-1071285439622810/*) and a Twitter account (*https://twitter.com/MakeRheum*) have been launched. Please visit both and encourage your undergraduate and internal medicine residents to visit and "like" them to find out more about rheumatology. Also, if you have material to post to the page, contact Virginia Hopkins at the CRA. Let's make rheumatology accessible to our students.

SickKids Rheumatology Recruits ready in their fight against rheumatic disease.

The next steps for TROT and *#MakeRheum* will be to expand the number of available opportunities for learner experiences in rheumatology across Canada. We encourage all programs to use the materials developed and to *#MakeRheum* for rheumatology!

Diane Crawshaw
TROT Project Coordinator,
Canadian Rheumatology Association
Hamilton, Ontario



CIORA 2016 Summary

By Janet Pope, MD, MPH, FRCPC

CIORA is issuing another call for grants in 2017! The CRA Research committee will be launching the 10th CIORA Grant Competition. The grant application deadline is March 31, 2017 and award winners will be notified at the beginning of June.

As we head into our 10th grant competition, we would like to recognize the CRA Research Committee members for their hard work and dedication. Thank you to Drs. Vinod Chandran, Alfred Cividino, Boulos Haraoui, Niall Jones, Laëtitia Michou, Mohammed Osman, Regina Taylor-Gjevre, Carter Thorne and John Wade.

We welcome back Dr. Paul Fortin as Review Panel Chair. Dr. Fortin provides valuable guidance and direction to our review panel. Past grant awardees are invited to be Review Panel members and to provide feedback on the process.

CIORA has had many successes this year. Here are just a few examples of how CIORA-funded research is materializing:

Poster Presentations

- Evaluating the Patient's Experience of the Diagnosis and Management of Psoriatic Disease (CRA 2016)
- #MakeRheum for Rheumatology: Pan-Canadian Working Group to Increase Interest in Rheumatology (CRA 2016)
- Pharmacologic Management of Takayasu's Arteritis: a Systematic Review (CRA 2016)
- Imaging Modalities for the Diagnosis and Disease Activity Assessment of Takayasu Arteritis: A Systematic Review and Meta-Analysis (CRA 2016)
- Effectiveness of a Telemedicine Education Program for Adults with Inflammatory Arthritis Living in Rural and Remote Communities in Ontario (BOOC 2016)

Published Literature

- Birth Outcomes in Women with a History of Juvenile Idiopathic Arthritis, *Journal of Rheumatology*
- A Prospective Comparison of Telemedicine Versus In-person Delivery of an Interprofessional Education Program for Adults with Inflammatory Arthritis, *Journal of Telemedicine and Telecare*

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Patient Tools

- Dynamic Computer Interactive Decision Application (DCIDA): Helping patients make better decisions.

CIORA's contribution to the advancement of rheumatology research in Canada is made possible by the unrestricted financial contributions of many industry partners. We would like to acknowledge their continuous support.

Janet Pope, MD, MPH, FRCPC
Professor of Medicine, Division Head,
Division of Rheumatology, Department of Medicine,
St. Joseph's Health Care, Western University
London, Ontario

CIORA: Call for Grants

CIORA is Issuing Another Call for Grants in 2017!

The CIORA Online Grant Application System opens January 30, 2017.

Letter of intent must be submitted by February 28, 2017.

The CIORA Online Grant Application submission deadline is March 31, 2017 at 23:59 Pacific Time.

Please visit *www.rheum.ca/en/research/* for more information.

Any questions can be directed to Virginia Hopkins at *virginia@rheum.ca*.

What the Heck is a Hackathon?

By John Esdaile, MD, MPH, FRCPC, FCAHS

You may well not have been to a hackathon yet as they are still a relatively new, but exciting, way to develop innovative technologies for politics, education, game design and most recently, healthcare. Google, Microsoft and NASA used a hackathon to develop software to help aid in disaster management and crisis response. The British Government held one to improve the lives of people with dementia. Eli Lilly Canada and Havas Life Manchester facilitated a hackathon in Vancouver, with 19 participants, who were either consumer-patients, consumer-patient advocates, nurses, physiotherapists, pharmacists, rheumatologists, scientists and knowledge-translation experts.

The goal was simple: To identify two key problems for patients and healthcare professionals dealing with rheumatoid arthritis (RA) and to develop functioning website prototypes to deal with these issues—in 30 hours, non-stop. Well, almost non-stop.

Identifying Problems and Challenges

Arthritis Consumer Experts set the hackathon stage by presenting an overview of the literature on identified and unidentified "gaps" in the consumer-patient journey with RA. Afterwards, several hours were devoted to focusing on two problems short-listed by the "hackers" through an iterative process—adherence to medication and unmet needs for patients. Small teams brainstormed ideas. More than 200 thoughts on how to solve these two problems were generated. The walls of the room were literally papered with sticky notes of endless sizes and colours.

Idea Reduction

With more than 200 ideas, there was a huge challenge to distill them into three or four main approaches. Incredibly, this was done. Three ideas were generated with the assistance of Havas Life magicians who had flown to Vancouver. Paper prototypes of the websites were developed. The teams sponsoring different ideas presented and, after considerable discussion, two ideas were selected:

(1) *Joint Partners:* This website is for real people living with RA to show others that they can succeed and should move forward with great hope. The concept was that no one could inspire people living with RA as well as peers and that fellow patients could be very convincing that a full life was possible despite RA. The website would provide a patient-to-patient support network where individuals could share their experience, hints and tips and find local support.

(2) *The RA Café:* The second website aims to help people integrate RA into their lifestyle and improve adherence. The concept was a one-stop resource for RA patients that would help them overcome the barriers to better health behaviours, and lead to better adherence and better outcomes. It would help patients in dealing with the many healthcare professionals they would interact with and provide high-quality, credible information as well as peer support and mentoring.

While those attending went to dinner, the Havas Life team that had flown to Vancouver from Manchester, England went to work.

The Magic begins

The time difference between Vancouver and Manchester allowed those in Vancouver to start working immediately on developing prototypes of the website. Around midnight, the Manchester team took over and continued the development process. Early the next morning, the Havas Life Vancouver team were able to present the new websites based on the paper prototypes. It was simply magical to see two strikingly different websites with many aspects already functioning. Everyone got the opportunity to play with the prototypes and make suggestions for the future.

Next Steps

It was an incredible experience to start one morning with empty walls and piles of blank sticky notes and to have two prototype websites 30 hours later. The Vancouver representatives and the unseen Havas Life team members in Britain made the impossible seem easy. Next steps will include external review, further focusing, additional refinement, and the hope will be that in the not too distant future at least one website will be launched that will help patients with RA help themselves do better and lead fuller, more confident lives.

Continued on page 9

Spreading the Word About Rheumatology at the Ontario Medical Students Weekend (OMSW)

By Jane Purvis, MD, FRCPC

The Ontario Rheumatology Association (ORA) Manpower Committee and the CRA human resources program, Training the Rheumatologists of Tomorrow (TROT), have been working together in various ways to increase the visibility of rheumatology to first-year medical students. Our most impactful activity thus far has been our participation at the Ontario Medical Students Weekend (OMSW). This annual event is held in one of the six medical school cities, and this year's event took place in London, Ontario, on October 14-15, 2016.

The ORA and CRA had a booth in the Medical Expo room and we greeted 550 first-year medical students in just one day! Students had the opportunity to speak to a rheumatologist to learn what rheumatology is all about and to try on gloves that simulate deforming rheumatoid arthritis. The students were given information on the CRA Summer Studentship opportunity, and they received information on how to contact the program directors at each of the medical schools, so they could pursue electives if desired. The *#MakeRheum* posters were on display as well as the now famous *RheumCareer* pens. We had the busiest booth in the room and were the only medical subspecialty in attendance. This continues to be a valuable opportunity to reach medical students early in their careers, so that rheumatology can be considered as the excellent career choice that we all know it to be.

Each year, a survey has been conducted to gauge the impact of the booth on the students who visit. The coordinator of the *#MakeRheum* campaign approached 30 students during the day to fill in a questionnaire regarding their experience. Both years the data have been striking!

This year, nine of 30 had heard about the subspecialty, and all of these students are considering an experience in rheumatology. A further 21 had not heard of rheumatology but, after visiting the booth, 18 said that they would consider pursuing an experience in rheumatology; two were undecided; and one indicated that he/she would not ("just would like some exposure now. My interest has been piqued"). That is, 90% of the undergraduate medical students who had a chance to hear about rheumatology from a passionate rheumatologist want an experience in rheumatology. We need to consider how to build capacity to satisfy this demand!

Jane Purvis, MD, FRCPC
Lead, Manpower Committee,
Past-president, Ontario Rheumatology Association
Rheumatologist
Peterborough, Ontario

What the Heck is a Hackathon? *(Continued from page 8)*

The Bottom Line

If someone invites you to a hackathon, say yes! It will be a lot of fun.

Thanks to Arthritis Consumer Experts for setting the hackathon stage by the consumer-patient perspective on the RA journey and to Eli Lilly Canada for supporting and driving this idea forward.

John M. Esdaile, MD, MPH, FRCPC, FCAHS
Professor of Medicine, University of British Columbia
Adjunct Professor, University of Calgary
Scientific Director, Arthritis Research Canada
Vancouver, British Columbia

News From the Scientific Committee

By Evelyn Sutton, MD, FRCPC

It seems only fitting, given the celebrations planned for Canada's 150th birthday, that the CRA's annual scientific meeting (ASM) will be held in our nation's capital. I am excited by our lineup of great speakers, workshops and, of course, for the time to network. The theme of this year's conference is sustainability—not just of the healthcare system—but also of individual and population health. You can expect the ever-popular Great Debate (*Biologics or Biosimilars? Be it Resolved That the Least Expensive Treatment Should be Chosen. Switch, Switch, Switch!*), scintillating workshops and given last year's success, Dr. Philip Baer's *RheumJeopardy*. A new session, *The Year in Preview*, should stir discussion; we are asking prescient experts to predict what breakthroughs 2017 will bring in basic science, clinical science, pediatrics and models of care.

The organizing committee and I are delighted that the following renowned speakers will be joining us:

Dr. Allen Steere, credited with the discovery of Lyme disease, has worked during the subsequent 40 years on studies of the clinical manifestations, epidemiology, pathogenesis, diagnosis, treatment and prevention of the infection. He serves as Professor of Medicine at Harvard and as Director of Translational Research in Rheumatology at Massachusetts General Hospital.

Dr. Matthew Warman is the Harriet M. Peabody Professor of Orthopedic Surgery and Genetics at Harvard Medical School. In 1994, Dr. Warman established an independent laboratory and clinical program in the Department of Genetics and Center for Human Genetics at Case Western Reserve University and University Hospitals of Cleveland. In 2006, he returned to Boston to become director of the Orthopedic Research Laboratories at Boston Children's Hospital.

Dr. Jonathon Fowles is a professor and exercise physiologist at Acadia University whose work in the Centre of Lifestyle Studies examines the effects of exercise on health in athletes, the elderly and persons with chronic disease or disability. Dr. Fowles has done extensive work with many organizations, such as the Canadian Diabetes Association, the Canadian Society for Exercise Physiology, the Heart and Stroke Foundation and many regional health authorities.

Do book your flights and hotel, and register for what promises to be a great meeting. I look forward to seeing you!

Evelyn Sutton, MD, FRCPC
Professor of Medicine and Medical Education,
Dalhousie University
Halifax, Nova Scotia

Update From the Education Committee

By Chris Penney MD, FRCPC

A chart audit workshop was held during the most recent Annual Scientific Meeting (ASM) in Lake Louise last February. Dr. Henry Averns was the prime mover of this initiative, but his flight was delayed due to bad weather. Dr. Mary Bell filled in for him at the last minute and did a superb job. Lessons learned from this workshop were used to develop the Chart Audit Library on the CRA website. Please go to *rheum.ca/en/members/chart_audit* for information on how to do a chart audit.

Remember to check the CRA website in 2017 for more practice improvement tools, such as the standardized transfer of care letter being developed by Dr. Mary-Clair Yelovich (internal medicine resident) under the supervision of Dr. Mary Bell.

If you've conducted a successful audit on your practice, we welcome your contribution for possible inclusion in the CRA Chart Audit Library. As you know, the Royal College requires us all to complete self-assessment (Section 3) activities, and this is an easy and inexpensive way to do this. Don't hesitate to send audit results to me for distribution

CRA Education Committee at the 2016 Lake Louise ASM

to the Education Committee for feedback and suggestions. Reflection on that feedback with resulting changes to your practice is an essential part of a successful chart audit.

If you have developed a continuing medical education (CME) self-assessment or practice reflection or improvement program that can be shared with your colleagues, please review the terms of reference for the Practice Reflection Award on the CRA website (*rheum.ca/en/the_cra/practice_reflection_award*). You may qualify for one of three awards given annually. The deadline for submissions is December 31, 2016. If you attended the Lake Louise ASM, you will have likely noticed the successful integration of the pre- and post-knowledge-transfer tests into the program. This is thanks to the work of CRA CEO Christine Charnock and her dedicated staff.

Finally, the Dilemma Rheum is a series of educational teleconferences designed for recently certified rheumatologists and trainees. Each session will feature an expert on a particular topic, who will discuss and answer questions on cases brought forward by participants. Special thanks are due to Dr. Janet Pope for piloting this program. Go to *rheum.ca/en/education/dilemma_rheum* for more information.

If you have ideas on education that you would like the CRA to develop or facilitate, please go to *rheum.ca/en/education/education_suggestion_box* and let us know.

Christopher Penney, MD, FRCPC
Associate Clinical Professor,
University of Calgary
Rheumatologist,
Richmond Road Diagnostic & Treatment Center
Calgary, Alberta

News From the Abstract Committee

By Maggie Larché, MBChB, MRCP(UK), PhD

The abstract committee is once again gearing up to review all of the submitted abstracts for the 2017 meeting.

We received 276 abstracts this year, covering a wide variety of topics.

In order to nurture trainees and young faculty, and foster enthusiasm amongst medical students and undergraduates, we have nine prizes to be awarded in 2017. These are:

- Best Abstract on Research by Young Faculty
- Best Abstract on Basic Science Research by a Trainee
- Best Abstract on Clinical or Epidemiology Research by a Trainee - *Phil Rosen Award*
- Best Abstract on Systemic Lupus Erythematosus (SLE) Research by a Trainee - *Ian Watson Award*
- Best Abstract by a Medical Student
- Best Abstract by a Postgraduate Resident
- Best Abstract by a Rheumatology Resident
- Best Abstract by an Undergraduate Student
- Best Abstract by a Postgraduate Research Trainee

Once again, there will be two interactive poster sessions for delegates to quiz the poster presenters and two podium sessions, which will include oral presentations of some of the best abstracts. Looking forward to seeing you there.

Maggie Larché, MBChB, MRCP(UK), PhD
Associate Professor,
Division of Rheumatology,
Departments of Medicine and Pediatrics
Staff Rheumatologist,
St. Joseph's Healthcare Hamilton and McMaster University
Hamilton, Ontario

Update From the Optimal Care Committee

By Cheryl Barnabe, MD, FRCPC, MSc

On behalf of the Optimal Care Committee, I'd like to first thank and acknowledge the contributions of Dr. Henry Averns as Committee Chair over the past four years. Dr. Averns led this committee in successfully advocating for changes to the Non-Insured Health Benefits (NIHB) formulary for access to biologics for Treaty First Nations with rheumatoid arthritis (RA) and overseeing several other activities, such as the finalization and dissemination of the Choosing Wisely campaign led by Dr. Shirley Chow and Dr. Carter Thorne; the CRA's involvement in the Wait Time Alliance led by Dr. Nigil Haroon; and the completion and dissemination of the Stand Up and Be Counted survey by members of the Human Resources Committee (in particular Dr. Claire Barber). We are very appreciative of Dr. Averns' commitment to remain the liaison to the NIHB going forward. CRA member responses to our NIHB Experience Survey were summarized and discussed with the NIHB in September, and we are now supporting the CRA membership with new resources to ensure that limited-use initial and renewal criteria are clear and accessible, as well as preparing a document so that the NIHB claims process is more understandable.

New activities within the Optimal Care Committee's scope were approved at the CRA Board Meeting in April 2016. In the next year, we will be focused on two specific efforts: (1) increasing the impact of rheumatologists' relationships with Indigenous patients through Indigenous cultural competency training; and (2) collaborating with Dr. Claire Barber and the Arthritis Alliance of Canada to determine a core data set for rheumatology, which will feed the collection of information relevant to the measurement of quality of care in our varied practice settings. The Optimal Care Committee is also participating in activities with the Guidelines Committee and will produce a summary document outlining processes suggested in the renewal of the RA Guidelines. I also represented the CRA at the Canada 2020 meeting in Ottawa in September, which served to discuss possible reforms and funding mechanisms for our health system as we enter another cycle of renewal of the Health Accord between the federal and provincial health ministries.

For more information, please visit *https://rheum.ca/en/members/clinical_resources*. The Optimal Care Committee is happy to receive your suggestions on activities that will fulfill our mandate to improve equitable access to quality care. Please contact myself at *ccbarnab@ucalgary.ca* or Claire McGowan-Shaw at *claire@rheum.ca*.

Cheryl Barnabe, MD, FRCPC, MSc
Associate Professor,
University of Calgary
Calgary, Alberta

WELCOME TO THE RHEUM & FAREWELL AS YOU LEAVE

Congratulations to:

Dr. Paul Davis and Dr. Brian Hanna as they embark upon retirement. The CRA and the *CRAJ* editorial board wish you both the very best.

Welcome to the following new members:

Tooba Ali, Hamilton ON
Amber Cogar, Winnipeg, MB
Ina Cusnir, Edmonton, AB
Martha Decker, Edmonton, AB
Muhammed Dhalia, Vancouver, BC
Caylib Durand, Calgary, AB
Shaina Goudie, Saskatoon, SK
Kun Huang, Richmond, BC
Sara Hussein, Montreal, QC
Konstantin Jilkine, Saskatoon, SK
Delphine Keyaert, Laval, QC
Sonia Lagacé Quebec, QC
Dara Mairiang, Vancouver, BC
Maig Nguyen, Winnipeg, BC
Marc-Etienne Parent, Sherbrooke, QC
Elisabeth Pek, Toronto, ON
Anthony Perruccio, Toronto, ON
Saara Rawn, Hamilton, ON
Alexandra Saltman, Toronto, ON
Michael Wokowski, Montreal, QC
Sophie Wojcik, Montreal, QC
Yan Yeung, London
Xiaxin (Tony) Zhang, Toronto, ON

CanREAL: How You Can Get Involved in Rheumatology

By Raheem B. Kherani, BSc (Pharm), MD, FRCPC, MHPE;
Susan Humphrey-Murto, MD, FRCPC, MEd; Christopher J Penney, MD, FRCPC

CanREAL is a subcommittee of the CRA Education Committee. CanREAL was founded on the premise of "promoting scholarship in rheumatology education" and stands for Canadian Rheumatology Education and Learning. About 15 years ago, Dr. Lori Albert originally convened a small nucleus of educators as an informal group. At the 2012 CRA Annual Scientific Meeting (ASM), the group met and formed this working group subcommittee. At the 2013 CRA ASM, the CRA provided official subcommittee status.

Purpose

- Promote exchange of ideas and best practices for rheumatology education at the undergraduate and postgraduate level;
- Promote scholarship in rheumatology education in Canada.

Membership structure:

There is an open committee membership of individuals interested in undergraduate and postgraduate medical education. A special welcome is extended to rheumatology trainees considering a career in medical education. Those interested in getting involved can contact:

- Dr. Raheem B. Kherani, Chair: *raheem.b.kherani@gmail.com.*
- Dr. Susan Humphrey-Murto, Vice-Chair: *shumphrey-murto-md@toh.on.ca.*
- Dr. Christopher Penney, Secretary and Chair, CRA Education Committee: *penney@ucalgary.ca.*

Meetings:

Face-to-face meetings are held at the CRA ASM each year. Teleconferences have been set up as needed throughout the year with the support of the CRA.

This is a national forum for collaboration in rheumatology education, innovation, and scholarship. Ongoing collaborations include developing shared projects and connections that the CRA fosters through the support of organizations such as CanREAL. There are plans to develop a new award, entitled the *Medical Education Innovation Project Award*, which would complement the recently developed *Practice Reflection Award*. Future directions include ongoing round-table discussions amongst rheumatology educators nationally to share best practices and innovations and to provide a platform for the development of scholarship across institutions. Through collaborations within the CRA, we are enhancing web resources and the educational delivery of the CRA ASM.

If you are interested in getting involved with medical education in rheumatology nationally, join us for the next CanREAL meeting in Ottawa!

Raheem B. Kherani, BSc (Pharm), MD, FRCPC, MHPE
Clinical Assistant Professor, University of British Columbia
Medical Lead, Arthritis Program,
GF Strong Rehabilitation Centre
Vancouver, British Columbia
Rheumatologist,
West Coast Rheumatology Associates
Richmond, British Columbia

Susan Humphrey-Murto, MD, FRCPC, MEd
Director of Education Research,
Department of Medicine,
University of Ottawa
Ottawa, Ontario

Christopher J Penney, MD, FRCPC
Associate Clinical Professor,
University of Calgary
Rheumatologist,
Richmond Road Diagnostic & Treatment Center
Calgary, Alberta

ORA Update

By Jane Purvis, MD, FRCPC

The Ontario Rheumatology Association (ORA) had another very successful annual meeting on May 27-29, 2016, at the JW Marriott in Muskoka. Attendance continues to be strong with more than 200 attendees from across the province. Dr. Janet Pope organized an excellent scientific program, with local and international speakers, which was interesting and thought provoking. Updates in scleroderma from Dr. D. Khanna, on gout from Dr. P. Khanna, as well as cardiovascular risks in inflammatory disease, and an update in dermatology were some of the topics covered. The keynote speaker was Suzanne McGurn, Assistant Deputy Minister and Executive Officer of Ontario Public Drug Programs, who discussed drug access in the province of Ontario.

In addition to scientific presentations, there were booths from various agencies in attendance and a very successful *Walk for the Arthritis Society* fundraiser, which raised more than $14,000. Educational activities on Saturday afternoon included photography, cooking demonstrations, wine tasting and a reptile presentation. Saturday evening included the gala dinner where Dr. Vandana Ahluwalia was awarded *Rheumatologist of the Year*, followed by dancing into the wee hours.

The ORA continues to flourish as a result of the commitment and enthusiasm of its executive, board of directors and the membership. The efforts of the group are seen not only in our annual meeting but in the various activities that we pursue throughout the year, and we hope to continue this throughout the years to come.

Our next annual meeting is on May 26-28, 2017, and it already looks like another excellent event.

Jane Purvis, MD, FRCPC
Lead, Manpower Committee,
Past-president, Ontario Rheumatology Association
Rheumatologist,
Peterborough, Ontario

Update From the AMRQ

By Frédéric Morin, MD

From one year to the next, I have the impression of announcing major changes in how medicine is practiced in Quebec! And so it is with 2017! Our busy Health Minister is tabling one bill after another in a carrot and stick game. To avoid cuts of up to 30%(!) in our income, we are being asked to accept a process of prioritized front-line access to specialized medicine, complete with performance targets. A single provincial form for rheumatology consultations will be implemented in early 2017. Appointments will then be made by a regional central authority, which means that we will need to give notice of availability three months in advance… We anticipate major disruptions from this bureaucratic entry and intrusion into our clinical practices. Despite everything, the Association des médecins rhumatologues du Québec (AMRQ) remains upbeat and is pursuing its own positive development. Our annual convention was held at the end of September and was a great success thanks to a synergistic association with members of the Société Française de Rhumatologie. Drs. Anne St-Pierre and Angèle Turcotte have ably prepared a Royal College section 3 credit program, called TOP 3 in rheumatology, which will be offered in spring 2017. Also in 2017, the AMRQ will be organizing a day focused on upgrading the skills of clinical nurses who work with our rheumatologists.

Finally, I would be remiss if I ended without congratulating my friend and colleague, Dr. Louis Bessette, on receiving the well-deserved 2016 *Merit Scholarship* from the AMRQ.

Frédéric Morin, MD
President,
Association des médecins rhumatologues du Québec
Montreal, Quebec

News From SOAR

By Volodko Bakowsky, MD, FRCPC

SOAR members at the annual meeting.

The 33rd annual meeting of the Society of Atlantic Rheumatologists (SOAR) took place at Fox Harb'r Resort near Wallace, Nova Scotia from June 17-19, 2016. Once again, rheumatologists from the three Maritime provinces convened for a weekend of intellectual and social development.

This year's David Hawkins Lecture in Rheumatology was given by Dr. Troy Torgerson, MD, PhD, from Seattle Children's Research Institute in Seattle, Washington. He opened the meeting with *How Do I Utilize the Lab to Evaluate the Immune system?* Following this, he gave a second talk *Immune Dysregulation Disorders—What Do They Look Like and How Do You Evaluate Them?* Dr. Torgerson has the unique ability to make a complicated subject matter approachable, and by the end of his talks we were all left enraptured.

Our second lecturer was Dr. Julius Birnbaum, MD, from Johns Hopkins in Baltimore, Maryland. He is the only dual-certified rheumatologist and neurologist in the United States. He spoke on the *Neurologic Complications of Lupus* followed by the *Neurologic Complications of Sjogren's*.

Lest you think it was all work and no play, there was some "down time" budgeted for the pursuit of non-medical expert roles such as golfing, running, tennis and fly-fishing.

We are all looking forward to SOAR 2017, which will once again be held at Fox Harb'r from June 23-25. Save the date!

Volodko Bakowsky, MD, FRCPC
Interim Division Head/Chief, Associate Professor
Division of Rheumatology, Department of Medicine,
Dalhousie UniversitPresident, Society of Atlantic Rheumatolgists
Halifax, Nova Scotia

WHEN METHOTREXATE ALONE IS NO LONGER ENOUGH, CONSIDER Pr XELJANZ®.

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XELJANZ (tofacitinib) in combination with methotrexate (MTX) is indicated for reducing the signs and symptoms of rheumatoid arthritis (RA) in adult patients with moderately-to-severely active RA who have had an inadequate response to MTX. In cases of intolerance to MTX, physicians may consider the use of XELJANZ as monotherapy.

Use of XELJANZ in combination with biological disease modifying anti-rheumatic drugs (DMARDs) or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Most serious warnings and precautions:

Risk of Serious Infections: Patients treated with XELJANZ are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, interrupt XELJANZ until the infection is controlled. Reported infections include: active tuberculosis, invasive fungal infections, bacterial, viral, and other infections due to opportunistic pathogens.

Treatment with XELJANZ should not be initiated in patients with active infections including chronic or localized infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Malignancies: Lymphoma and other malignancies have been observed in patients treated with XELJANZ. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with XELJANZ and concomitant immunosuppressive medications.

Other relevant warnings and precautions:

- Risk of gastrointestinal perforation. Use with caution in patients who may be at increased risk for gastrointestinal perforation.
- Risk of viral reactivation, including herpes zoster.
- Risk of malignancies, lymphoproliferative disorder, and nonmelanoma skin cancer.
- Risk of lymphopenia, neutropenia, anemia, and lipid elevations.
- XELJANZ should not be used in patients with severe hepatic impairment, or in patients with positive hepatitis B or C virus serology.
- Use with caution in patients with a risk or history of interstitial lung disease (ILD).
- XELJANZ can increase the risk of immunosuppression. Concurrent use with potent immunosuppressive drugs is not recommended.
- Concurrent use with live vaccines is not recommended.
- Use with caution in patients with impaired renal function (i.e., CrCl <40 mL/min).
- XELJANZ should not be used during pregnancy.
- Women should not breastfeed while being treated with XELJANZ.
- The safety and effectiveness of XELJANZ in pediatric patients have not been established.
- Caution should be used when treating the elderly and patients with diabetes because of an increased risk of serious infections.
- Use with caution in Asian patients because of an increased risk of events including: herpes zoster, opportunistic infections and ILD.
- Treatment with XELJANZ was associated with increases in creatine kinase.

Pfizer

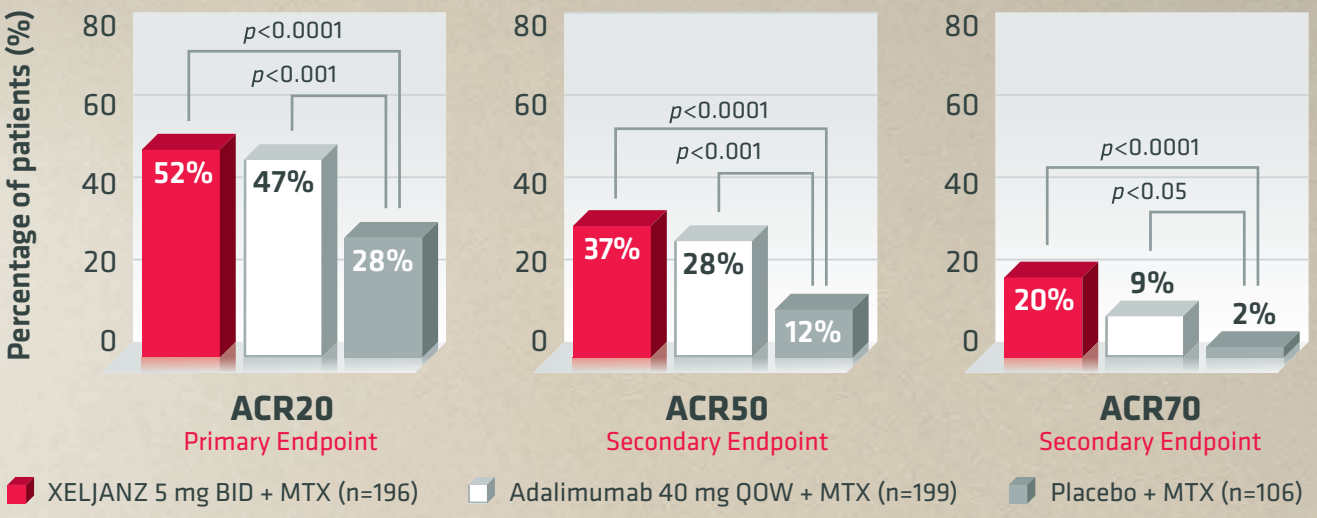
CA0116TOF024E

Demonstrated efficacy where response to methotrexate was inadequate

In MTX-IR patients, XELJANZ + MTX showed significantly greater symptom reduction vs. placebo + MTX at 6 months (as measured by ACR response rates).[1*]

This study was not designed to compare XELJANZ to adalimumab.

ACR response rates at 6 months



Improvements from baseline in physical functioning were significantly greater in patients receiving XELJANZ + MTX vs. placebo + MTX at 3 months (as measured by decreases in HAQ-DI scores).[1*]

Mean HAQ-DI decrease from baseline at 3 months: -0.56 XELJANZ 5 mg BID or -0.51 adalimumab 40 mg QOW vs. -0.25 placebo ($p<0.0001$).
This study was not designed to compare XELJANZ to adalimumab.

- XELJANZ causes a decrease in heart rate and a prolongation of the PR interval. Caution should be observed in patients with a low heart rate at baseline (<60 beats per minute), a history of syncope or arrhythmia, sick sinus syndrome, sinoatrial block, atrioventricular (AV) block, ischemic heart disease, or congestive heart failure.
- Treatment with XELJANZ was associated with increased incidence of liver enzyme elevations.

For more information:

Please consult the Product Monograph at http://pfizer.ca/pm/en/XELJANZ.pdf for important information relating to adverse reactions, interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling us at 1-800-463-6001.

Reference: 1. Pfizer Canada Inc. XELJANZ Product Monograph. September 15, 2015. **2.** Arthritis Society. June 2014 Impact - Ease of Use. Available at http://www.arthritis.ca/page.aspx?pid~7650. Accessed July 22, 2014.

BID = Twice daily; QOW = Every other week; MTX-IR = Methotrexate Inadequate Responders

* Multicentre, randomized, double-blind, placebo-controlled study in patients ≥18 years with active RA according to ACR criteria. Patients received MTX and were randomized to receive XELJANZ 5 mg BID (n=196), adalimumab 40 mg QOW (n=199), or placebo (n=106). The primary endpoints were the proportion of patients who achieved an ACR20 response at month 6, mean change from baseline in HAQ-DI at month 3, and the proportion of patients who achieved DAS28-4 (ESR) <2.6 at month 6.

† The Arthritis Society's Ease-of-Use Commendation recognizes products, like the XELJANZ bottle cap, that have been independently tested for easy use and handling for people living with arthritis. The Arthritis Society does not determine the therapeutic value of products and the designation is not intended as a general product endorsement that are designed for ease of use in patients with arthritis.

The XELJANZ bottle cap was awarded The Arthritis Society's Ease-of-Use Commendation.[2†]

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News From the Arthritis Alliance of Canada (AAC)

By Jaime Coish, Executive Director, AAC

The Arthritis Alliance of Canada (AAC) is a Pan-Canadian assembly of more than 30 arthritis stakeholder organizations who share a common goal—to improve the lives of Canadians with arthritis.

AAC Annual Meeting

On October 27-28, 2016, the AAC hosted its annual meeting, "Translating Arthritis: Knowledge to Action for Canadians," in Montreal, with its partners, the Canadian Institute of Health Research (CIHR) Institute of Musculoskeletal Health and Arthritis (IMHA) and The Arthritis Society. The event brought together arthritis healthcare professionals, researchers, funding agencies, government affiliates, voluntary sector agencies, industry, trainees and arthritis patient representatives who worked collectively, over two days, to advance our national framework through our three key pillars: 1) advocacy and awareness; 2) research; and, 3) improving prevention and care. Workshop presentations and a welcome remarks video from MP Yves Robillard, in support of arthritis, are available at *http://arthritisalliance.ca/en/events/annual-conference*.

AAC Research Awards Program

Launched October 27, 2016, at the AAC Annual Meeting Gala Dinner, the new awards program will recognize national high-quality research in AAC priority areas as identified in the National Framework. This recognition will: 1) formally acknowledge the outstanding contributions of patient partners and scientists; 2) help researchers in competing for and participating in national grants and programs; and 3) provide opportunities to highlight arthritis research.

A total of seven awards will be granted, valued at $750 CAD per award, generously sponsored by AAC members, as follows:

Four awards for trainees/early career researchers/early career faculty members/investigators for their contributions to arthritis research, and one award for each of the following levels:

1. Masters Student, sponsored by the McCaig Institute for Bone and Joint Health
2. PhD Student, sponsored by Arthritis Consumer Experts
3. Post-doctoral fellow, sponsored by the CIHR Institute of Musculoskeletal Health and Arthritis
4. Young faculty researcher (graduate within the first five years), sponsored by the CIHR Institute of Musculoskeletal Health and Arthritis
5. Knowledge-Translation (KT) research, sponsored by the Bone and Joint Institute of the University of Western Ontario (open to all investigators at any career level)
6. Knowledge-Translation (KT) practice, sponsored by Janssen, Inc. (open to all investigators at any career level)
7. Patient for active engagement in arthritis research, sponsored by The Arthritis Society.

Deadlines:

- Full applications received to AAC office *lgazizova@arthritisalliance.ca* by Tuesday, January 3, 2017 (midnight ET).
- Decisions to be announced early March 2017.
  Please visit *www.artrhitisalliance.ca* to access the applications, guidelines and details.

We all have a role to play in improving arthritis prevention and care in Canada. A huge thank you to AAC Members, for their commitment and contributions. Without their support, these important initiatives would not be possible. Their ongoing work both as individual organizations and in collaboration with other arthritis stakeholders is essential to achieving the overall goal of mitigating the burden of arthritis.

To receive our monthly newsletter to stay informed or get involved, please contact Jaime Coish at *jcoish@arthritisalliance.ca*.

Jaime Coish
Executive Director, Arthritis Alliance of Canada
Toronto, Ontario

Notes From the NWRS Meeting

By John P. Wade, MD

The 2016 Northwest Rheumatism Society Meeting (NWRS) was held in Vancouver on May 5-7, 2016. This international meeting is held annually, rotating between Portland, Oregon; Seattle, Washington; and Vancouver, British Columbia. The local organizing committees put on a two- to three-day educational meeting that has been successfully running for many decades to foster learning and provide an opportunity for collaboration between rheumatologists in the Pacific Northwest. The U.S. states include Oregon, Washington, Idaho, Montana and Alaska. Western Canadian provinces are also represented and consist of Manitoba, Saskatchewan, Alberta and British Columbia. In recent years, the meeting has grown to be recognized as a premier educational event.

The 2016 meeting started with a state-of-the-art lecture on spondyloarthropathies given by Dr. Walter Maksymovych from the University of Alberta. There was emphasis on the current clinical appreciation of the spectrum of the disease, recent classification and treatment options. The following morning started with an update on the role of stem cell transplants for rheumatic diseases given by Dr. Sharon Le Clerq and Dr. Jan Storek from the University of Calgary. Our patients who have a poor prognosis might be considered for transplantation if no other therapies are available. A review of imaging for rheumatologists, by Dr. John O'Neill from McMaster University, emphasized the important role of imaging, highlighted the radiation risks and discussed newer imaging modalities.

Dr. Mollie Carruthers, who has recently joined our group from Harvard University, brought us up to date on the spectrum of IgG4-related disease. This was followed by two provocative talks, by Dr. Desiree van der Heijde and Dr. Robert Landewe of Europe, covering where we are with imaging for remission in rheumatoid arthritis (RA), and recent trials that suggest that ultrasound may not be as good as promised for assessment of our patients as an aid in clinical decision-making.

An outstanding lecture on newer approaches to serological diagnosis of auto-inflammatory and systemic rheumatic diseases, by Dr. Marv Fritzler, highlighted the importance of using the laboratory to better characterize some of our diseases.

This was followed by a Thieves Market where rheumatology fellows from the University of British Columbia stumped senior clinicians with rare rheumatologic cases.

Dr. Monika Ostensen from Sweden gave a state-of-the-art lecture on management of patients with rheumatic diseases in pregnancy. Following this was an eloquent discussion on structural damage in RA and psoriatic arthritis (PsA) by Dr. Georg Schett from Germany, who laid the foundation for a subsequent clinical discussion of management of these important diseases in rheumatology.

The keynote address, *Autoimmune Inflammatory Disease: Moving Towards Prevention* was given by Dr. Paul Emery from Leeds University. His lecture highlighted that while we are currently successful with established disease, we now have to set the bar higher to identify disease before damage has occurred and utilize earlier strategies in management.

The meeting ended with an excellent "year in review," by Dr. John Watterson, on the landmark papers in rheumatology in the prior 12 months.

John P. Wade, MD
Medical Director
Pacific Arthritis Centre
Vancouver, British Columbia
University of British Columbia

Dr. Paul Emery at the NWRS meeting.

Why I Muck

By Erin Norris, MD, FRCPC

I was diagnosed with multiple sclerosis (MS) in 2010, when I was 20 weeks pregnant with my third child. When Leah was born, I would watch her and wonder if I would be able to do all that I did with her older siblings. And when I was ready to stop wondering, I decided to do something to make it happen.

In 2014, I participated in my first Muck MS Canada event in Hamilton. I had never done an obstacle course event before, but it seemed different and challenging. My husband, Larry, was incredibly supportive and joined my team right away. I convinced our friends, Anthony and Naomi, to join us too, although I'm sure they both thought I was slightly crazy.

As donations from friends and family rolled in, I realized that I was really going to have to do this. The night before the Muck, I lay awake thinking about the obstacles that would be insurmountable and that my left leg might give out on me. I had trained and I was ready, but I worried about the unpredictability of my body when I challenged it.

But the next day, the energy and camaraderie at the event were outstanding. I saw strangers help each other through, over and under obstacles, and teammates that cheered each other on. Adrenaline propelled me through the course, and my heart was ready to burst with pride as I crossed the finish line to applause and leaned forward to receive my medal. I was proud of what I had accomplished, and grateful that so many people were there, for me and for others, in the fight to end MS. I'm only a little embarrassed to admit I cried.

I have now participated in three Muck MS events. This year, my family and my team pledged to fundraise $100,000 for the MS Society of Canada by "mucking" it up. I am proud to be raising both MS awareness, and funds to support MS research. Three years later, I know that the obstacles awaiting me on the course—like the challenges of MS—won't defeat me.

For more information on Dr. Norris's fundraising efforts visit her website at http://mssoc.convio.net/goto/ErinNorris2016.

Erin Norris, MD, FRCPC
Assistant Professor, University of Toronto
Staff Rheumatologist, Division of Rheumatology
St. Michael's Hospital
Toronto, Ontario

Dr. Norris's family and team pledged to raise $100,000 for the MS Society of Canada.

Dr. Norris and her husband "mucking" it up at the MUCK MS event in Hamilton.

Photos credited to MS Society

Finding Work-life Balance the Hard Way

By Erin Norris, MD, FRCPC

I am five months pregnant with my third child, scrolling through patient labs on my office computer. The summer sun streams in from a window on my right side, which must be why I can't see the screen very well. Except that over the next three days, I can see less and less out of my right eye, until I can barely count fingers. The ophthalmology resident on call meets me in the hospital on a Sunday. There is a flurry of specialists, an urgent MRI, and I am diagnosed with multiple sclerosis (MS). I am fine until I'm not: my daughter is eleven months old, and I develop severe vertigo and ataxia. I can't go to work. I can't even carry my daughter.

Photo credit: Kelly Fischtein

Dr. Norris and her family (pictured from left to right): Her daughter Rebecca, Dr. Erin Norris, her son Judah, her husband Larry, and her daughter Leah.

MS isn't really that different from any of the chronic, unpredictable diseases that we treat as rheumatologists. There is uncertainty, denial, and fear—a betrayal of the body. There is an indignity, a loss of control, which comes with being a patient. Does all this really make me a better doctor? When I return to work, I am slower, I see fewer patients, and I hold fewer clinics. I stop taking hospital calls, and my colleagues have to pick up the slack. I transfer care of my most acute (dare I say interesting?) patients, and some patients request transfers because they wait too long to see me.

And yet, I listen more. I take more time. I understand the small injustices of being a patient—especially the waiting—and the bigger ones, too. I know deeply that what patients discuss in the physician's office is such a small piece of their illness experience and of their person. So I try to honour this. I try to be the kind of patient advocate I want for myself. And in this way, I bring back my feeling of self-worth as a physician.

Here is the truth: I will never be the right rheumatologist for every patient. But I can be a great rheumatologist for some patients. And, by adapting my practice, I have enough left to also be a great wife and mother—because, really, I am the only mother my children have, and my husband's only wife. I never would have chosen this work-life balance, but I can finally say I am grateful for it.

Erin Norris, MD, FRCPC
Assistant Professor, University of Toronto
Staff Rheumatologist, Division of Rheumatology
St. Michael's Hospital
Toronto, Ontario

My Decision to Pursue Rheumatology

By Natalia Pittman, MD, FRCPC, MSc, BSc

My decision to enter rheumatology happened unexpectedly. My line of sight had always, even before entering medical school, been on medical oncology. I had many inadvertent opportunities in rheumatology prior to choosing my specialty that eventually led me to change my career focus.

During the completion of my undergraduate degree at Memorial University, I was involved in exciting research in the areas of ankylosing spondylitis and psoriatic arthritis. While in medical school, I tried to secure a rotation in general internal medicine (GIM) or medical oncology for an upcoming elective at Queen's University in Kingston, Ontario; however, I was unable to secure placement in one of these areas. They were able to accommodate me for an elective in rheumatology, which I begrudgingly accepted.

My experiences during this elective made me question my decision to pursue medical oncology. I quickly realized that there were many facets to rheumatology that I enjoyed and that I could relate to. I was, and still am, fascinated with the complex and often unusual presentations of the diseases. I enjoy the challenge of arriving at a diagnosis and the subsequent management strategies given the new advances in biologic medications. I was able to quickly recognize the strong and ongoing doctor-patient relationships that existed in this specialty and was pleased to see how the addition of the appropriate treatment plan could ensure a quality of life to those patients impacted by rheumatologic conditions.

Skipping ahead several years, it has been six months since my transition from an internal medicine resident at Queen's University to a rheumatology fellow at McMaster University, and with that came many challenges. In pursuit of rheumatology training, my family and I made the decision to move from a city that we called home to a city that was unknown to us. Not only did I have to acquaint myself with a new area, I also had to familiarize myself with a new work environment: four hospitals, new staff and colleagues, and new electronic medical record systems. This was all very overwhelming. A welcome change was home call, which is certainly a nice break from the in-house call that I was accustomed to as a GIM resident and allowed me to spend more time with my husband and two children.

Despite the excitement of starting this new chapter in my personal and professional life, I also felt some anxiety. I had significantly increased responsibility and accountabilities as a perceived 'expert'. I was no longer a resident, but rather became junior attending for my patients, and a teacher and resource for medical students and residents. My confidence grew during my first few weeks as a rheumatology fellow because of supportive staff and an environment that fostered learning. I also had the opportunity to attend the Basic Skills Course for the Rheumatology Fellow in Vancouver, B.C., which was a week-long course that helped prepare me for fellowship.

I quickly realized that there were many facets to rheumatology that I enjoyed and that I could relate to.

Right now, my challenge lies with balancing the need to learn rheumatology whilst studying for the Internal Medicine Royal College exam. My work-life balance has shifted more to just work. It has proven to be the most challenging time of my life given the time commitments of studying on top of work demands and personal life. Thankfully the support of my family has allowed me to focus on these multiple competing priorities. Through it all, there is one thing that I am sure of; I chose to enter a specialty in which I can see myself having a long and rewarding career and one I can say I truly enjoy.

Natalia Pittman. MD, FRCPC, MSc, BSc
Rheumatology Fellow
McMaster University
Hamilton, Ontario

How to Analyze Clinical Trial Research in Rheumatology

By : Philip Baer, MD, MDCM, FRCPC, FACR*; Michael Starr, MD†; Nigil Haroon, MD‡

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Introduction

Rheumatology is a rapidly changing specialty with hundreds of clinical trials being published in the field every year. It is nearly impossible to keep up with the literature, and almost as difficult to discern which trials provide valuable new knowledge, and which have little to offer the practising rheumatologist.

The goal of this article is to help solve this problem. We will briefly describe the characteristics of well- and poorly-designed trials thereby serving as a guide to identify when a trial's design, analyses, or conclusions suffer from errors that range from poor choice of patient populations to misidentification of a class effect among agents. A checklist has also been created that can be used to quickly assess new research reports and assist in interpreting their conclusions.

Study Design

Depending on the type of clinical evidence available, the risk of bias varies. It is important to be aware of the level of clinical evidence before interpreting the results. Based on the level of evidence available to answer a particular clinical query, or research question, the strength of recommendations varies. This is universally accepted and recently the Canadian Rheumatology Association (CRA) rheumatoid arthritis (RA) guidelines used the same grid (Table 1).

Type of study. Prospective trials look forward and track the development of outcomes over time in their chosen populations. Retrospective trials look backward at past records to determine whether certain risk factors or past interventions that differed between two groups influenced specific outcomes. Although retrospective trials can produce useful long-term data, certain kinds of bias are more common in retrospective than in prospective studies, and this can affect the validity of their results.[2,3] In addition, retrospective studies may lack necessary baseline parameters that are required to be controlled to assess independent effects.[3] For example, a retrospective examination of septic arthritis as a complication of RA over 35 years was done at a single centre, but information on disease activity, functional out-

Table 1:
System for Assigning Level of Evidence and Strength of Recommendation[1]

Levels of Evidence	Strength of Recommendation
I. Meta-analyses, systematic reviews of RCT, or individual RCT	A. Strong recommendation: • Direct level I evidence
II. Meta-analyses, systematic reviews of observational studies (cohort/case control studies), or individual observational studies	B. Moderate recommendation: • Direct level II evidence or extrapolated level I evidence
OR	
RCT subgroup/post hoc analyses III. Nonanalytic studies, eg., case reports, case series	C. Weak recommendation: • Direct level III evidence or extrapolated level II evidence
IV. Expert opinion NR Recommendations are not linked to evidence	D. Consensus recommendation: • Expert opinion based on very limited evidence

RCT = randomized controlled trial; NR = not reported.

comes, and structural damage, factors that could affect the outcome, were not available for most patients.[4]

Randomization and blinding are excellent methods to minimize bias. If patient allocation to treatment groups is not randomized, investigators may inadvertently place patients who are sicker into the treatment group they believe is more effective. If the study is not blinded, patients, investigators, and outcome assessors may overestimate treatment effects, especially for subjectively assessed outcomes.[5] Both lack of randomization and nonblinding have been associated with an increased likelihood of a new therapy being found to be superior to its comparator.[6]

Even randomized controlled trial results obtained by post hoc or subgroup analyses are subject to bias.[7,8] A post hoc analysis examines the data after the trial is completed and reports on end points that were not prespecified in the study design. It has been suggested that not disclosing to the reader that an analysis is post hoc should be considered scientific misconduct.[9]

Subgroup analyses involve analyzing the data in specific patient groups (divided by age, sex, disease severity, or other factors) to see whether a treatment worked particularly well in a particular type of patient. Unfortunately, if enough subgroups are specified, the likelihood of a false positive result increases: carrying out 10 subgroup analyses results in a 40% chance of at least one producing a false positive result at the $p < 0.05$ significance level.[7] A correction factor for multiple comparisons, such as the Bonferroni correction, should be used in this situation.[10]

Patient population. Clinicians can apply the results of a trial to patient care only if the trial patients resemble those seen in clinical practice. The first table in a clinical trial report usually summarizes the characteristics of the patient population, including age, sex, disease severity and/or duration, comorbidities, and medication history. Ideally, trial patients should be similar to practice patients in most of these respects. In particular, trial results observed in patients who are more or less ill, in a different age group, of a different sex, have more or fewer comorbidities, or have failed more or fewer previous medications are less likely to be applicable to all patients with the studied condition. Check for allowed rescue therapies and concomitant medications as well as baseline differences between the treatment groups. It has been estimated that only 5% of patients seen in typical rheumatology clinical practice would be eligible for RA clinical trials based on common inclusion and exclusion criteria.[11]

Decisions around patient recruitment techniques may result in a skewed patient population. For example, a recent low back pain trial recruited all patients from a single back pain clinic in a tertiary hospital.[12] A patient population from such a specialized setting may not reflect the average Canadian clinician's practice in terms of sociodemographic characteristics, lifestyle factors, or circumstances, and the trial's results may therefore not apply to patients outside this small population.

To avoid this limitation, large trials often recruit patients from a wide range of centres, ideally in different parts of the world. However, this carries its own risk of lack of standardization of both the intervention and the end point measurements. In addition, trials done in areas with poor access to health care may show higher than usual placebo response rates due to patients remaining in the trial in order to access otherwise unavailable medical care. (P. Baer, personal communication, June 15, 2016) Risk profiles reported in studies conducted in populations with higher rates of geographically endemic conditions, such as tuberculosis or hepatitis, may not be applicable to other populations.

Sometimes a trial is designed to include only patients in a certain age or disease severity category. For example, although the original Trial of Etanercept and Methotrexate With Radiographic Patient Outcomes (TEMPO) included RA patients with any level of disease severity if they had failed a disease-modifying antirheumatic drug (DMARD) other than methotrexate,[13] a TEMPO extension study included only patients with moderate disease.[14] While this was clearly disclosed, it does mean that the study's results are not necessarily as applicable to patients with mild or severe disease.

Similarly, the RAPID-axSpA trial studied certolizumab in patients with axial spondyloarthritis and found significant benefit compared to placebo. However, the study only recruited patients with a C-reactive protein (CRP) above 7.9 mg/L and/or sacroiliitis on MRI according to the ASAS/OMERACT definition, so its results can only be applied to patients with those characteristics.[15]

Study populations also need to be large enough to detect a real difference between treatments if one exists; otherwise, a negative result may be meaningless, and the trial misleading to clinicians looking for information applicable to their practices. The number of patients needed to detect a difference depends on the frequency or variability of the outcomes being measured and the expected effect of the intervention(s) being studied, among other factors,

and statisticians have developed formulas (power calculations) to calculate it.[16,17] However, because patient recruitment can be more difficult than expected, studies may be underpowered and conclude, erroneously, that there is no difference between treatment arms (type 2 error). Furthermore, trials rarely perform power calculations for subgroup analysis, leaving them frequently underpowered and at an even greater risk of false-negative results.[18]

This was a significant issue for rheumatology trials in the past[19] but may still occur. For example, a 2012 trial of combined physiotherapy and acupuncture in patients with severe knee osteoarthritis awaiting surgery found no benefit over usual care, but the required sample size was not achieved.[20] A 2014 trial comparing etanercept plus methotrexate with various DMARDs plus methotrexate did not achieve a significant difference in some of its end points due to patient attrition that led to underpowering.[22]

Similarly, the ABILITY-1 trial for nonradiographic axial spondyloarthritis (nrAxSpA) excluded patients who fulfilled the modified New York criteria for ankylosing spondylitis (AS).[21] However, central post hoc reading of 102 patient X-rays led to reclassifying 38 patients as indeed fulfilling these criteria. Since the trial included only 185 patients, the reclassification of such a large proportion resulted in low power and the US Food and Drug Administration's Arthritis Advisory Committee rejected an application to extend the indication for adalimumab to include patients with nrAxSpA.[23]

Interventions. In non-placebo-controlled trials, the choice of comparator is vital: a comparison with an intervention less effective than the standard of care for the condition being treated will not accurately demonstrate the tested agent's clinical usefulness.[24] The ADACTA trial is an example of the issue involved. This trial showed that tocilizumab monotherapy was superior to adalimumab monotherapy in patients with RA. Adalimumab was chosen because it was "a globally adopted, first-line biological therapy (in combination with methotrexate and as a monotherapy) in patients with rheumatoid arthritis who are refractory to nonbiological disease-modifying antirheumatic drugs."[25] However, the known efficacy of tocilizumab as a monotherapy agent, as opposed to the usual use of adalimumab in combination with methotrexate, must be considered when reviewing the trial outcomes.

To be useful in clinical practice, trials also need to reflect commonly used and/or approved doses of both the drug being tested and its comparator(s). For example, a psoriatic arthritis (PsA) trial compared 7.5–15.0 mg of methotrexate weekly to placebo in order to determine the efficacy and safety of low-dose methotrexate. The trial reported no significant difference in the number of swollen and tender joints with methotrexate use. However, given that the dose selected was markedly lower than what is commonly used in clinical practice, the trial's results are not truly applicable to Canadian physicians.[26]

Similarly, a low back pain trial compared celecoxib 400 mg/day (the maximum recommended daily dose) with acetaminophen 1,000 mg/day (the maximum recommended dose is 3,200–4,000 mg/day).[12] It is not surprising that celecoxib showed superior effects on pain. Another example is the SATORI trial in RA, which compared tocilizumab with methotrexate 8 mg/week—a dose much lower than is usually used in North America.[27]

Note that even placebo-controlled trials can have inherent bias, since route of administration has the potential to influence how effective an intervention is perceived to be by participants.[28,29] Whenever possible, well-designed trials will ensure all treatment arms, including placebo, are administered via the same route.

End points. Study end points need to be carefully defined in order to produce valid results. Disease activity scores, American College of Rheumatology (ACR) responses, and blood test results have predetermined criteria that improve their reproducibility, but more subjective end points, such as assessments of functional limitation, disease activity, or quality of life, may by fuzzier and subject to disagreement. Surrogate measures, such as biomarker levels, may be erroneously accepted as disease outcomes even when they are less meaningful than primary outcomes such as remission. Unvalidated end points (such as the use of spondyloarthritis measures like Spondyloarthritis Research Consortium of Canada [SPARCC] scores in a mechanical back pain study[12]) may not correlate with disease activity in conditions other than those they were designed for.

End points also need to matter in the sense of reflecting a true change in a patient's well-being. For example, RA trials often include erosion measurements, and though minimal clinically important differences have been established, the clinical implications of small differences in erosion scores, even when statistically significantly different from the comparator, are not always clear.[30] When possible, prior to study initiation, questionnaires should be validated in the condition being studied to confirm that a positive result truly correlates with a change in the patient's condition.

End points should also reflect an appropriate level of follow-up for the condition being treated. Early results may either underestimate or overestimate long-term treatment results. In particular, studies using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) to measure radiographic damage in AS need long-term follow-up to see useful results.

Finally, end points may include adverse events, and the way they are reported is important. Event rates can be exaggerated or downplayed by being expressed differently: as a percentage of all patients, as absolute numbers, as numbers per 100 patient-years, and so on. Make sure the event rates include events from the entire duration of the trial, since not all events have an acute onset.

Results

The first diagram in a trial report is often a patient flow diagram showing the numbers of patients recruited, excluded from participation, randomized into each treatment group, and followed up at specified time points (Figure 1). This useful diagram provides a quick way to look at how the study population changed over time and determine how many of the enrolled patients are actually included in the results.

Study Design

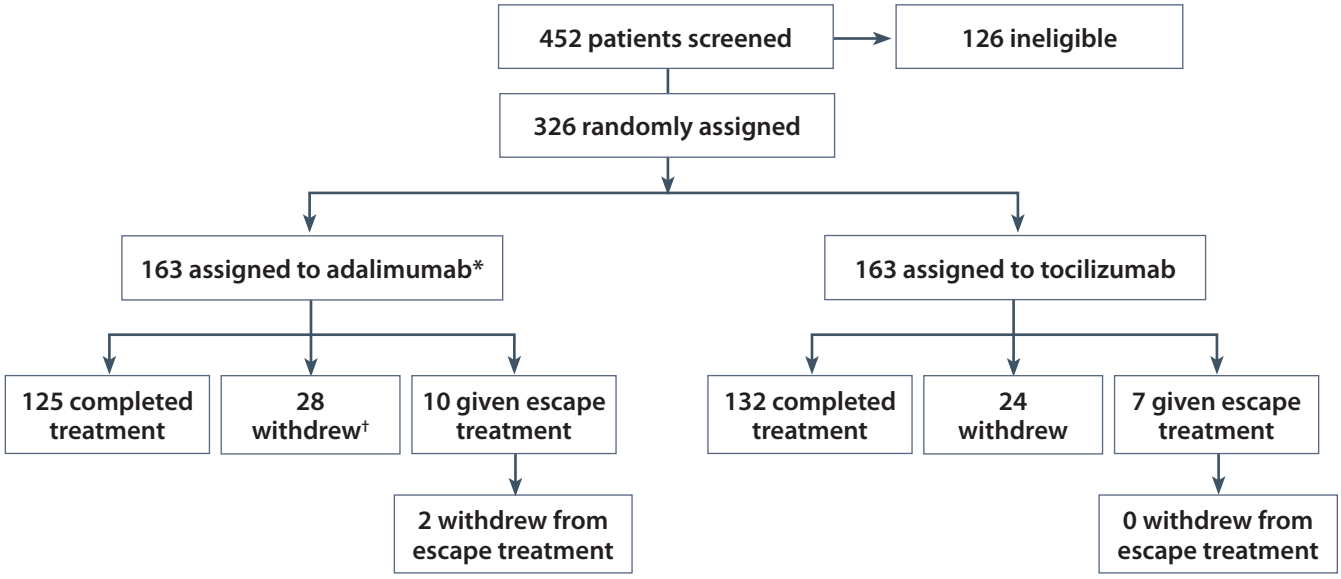
- ☐ Was the trial prospective?
- ☐ Was the trial randomized and double-blind?
- ☐ Were the end points reported those originally specified in the study design?
- ☐ Did all the patients actually have the condition being studied?
- ☐ Were the baseline characteristics similar between groups?
- ☐ Were the patients involved similar to those you see in your practice?
- ☐ Was the study population large enough to detect differences between treatments?
- ☐ Did the comparator represent the standard of care?
- ☐ Was the comparator dosed in the commonly used/approved way?
- ☐ If the comparator was placebo, was the route of administration the same as the active treatment?
- ☐ Were the end points objective or, if subjective, measured with validated instruments?
- ☐ Had all surrogate end points (such as blood levels) been previously demonstrated to correlate with disease activity?
- ☐ Were the end points measured at clinically relevant times and was the follow-up period long enough to capture clinically meaningful outcomes?
- ☐ Did all the end points reflect clinical differences in patient well-being?
- ☐ Did the adverse event rates include events from the entire trial duration?

Additional Considerations for Subgroup Analysis

- ☐ Was the subgroup analysis predefined or carried out post hoc?
- ☐ Would eligibility criteria, investigator assumptions, or gold standards used as part of original study affect results of the analysis?
- ☐ Were sample size calculations completed to ensure sufficient power for subgroup analyses?

*The more questions you can answer with a "yes," the better the quality of the trial and its reporting.

Figure 1:
Example of a Patient Flow Diagram



*One patient in the adalimumab group who did not receive study treatment was not included in the intention-to-treat population. †Does not include the two escape patients who withdrew.

Figure 1. A good example of a patient flow diagram from the ADACTA trial, although details of the reasons for patient withdrawals would improve it.[25]

Analyzing the data. An intent-to-treat (ITT) analysis looks at the results for all patients randomized to any treatment group, even if they never receive treatment. This is the least biased method of analyzing trial data.[31-33] However, some investigators instead do an as-treated analysis, which compares patients based on what treatment they actually received, or a per-protocol analysis, which uses only the data from subjects who met all the protocol criteria and completed their assigned treatments. Not only can the reduced sample sizes resulting from these approaches cause a loss in statistical power to detect treatment differences, but the benefits of randomization are lost.[34]

Missing data from patients who dropped out can be handled in various ways. A rigorous approach is nonresponder imputation, which assumes that all subjects with missing data didn't meet the study end points. Another is imputation, where the subject's other responses are used to estimate the missing data point(s), although it is impossible to check the accuracy of these estimates. A third is last-observation-carried-forward (LOCF) analysis, which uses the subject's most recent data point in place of the missing one. This is a common approach, but since a key reason for patients to drop out is lack of clinical benefit, LOCF analyses tend to inflate the success rates of all treatment arms.

An even more rigorous approach than nonresponder imputation was used by the Oral Rheumatoid Arthritis Phase 3 Trials Standard (ORAL Standard) study, comparing tofacitinib, adalimumab, and placebo in RA.[35] Patients were assessed for nonresponse after 3 months, and nonresponding placebo patients were advanced to active therapy. However, nonresponding patients at 3 months in an active treatment group were not eligible to be categorized as responders at the primary end point assessment at 6 months, even if they had become responders by that time. This is called nonresponder imputation with advancement penalty. The same design was used in the FUTURE 2 trial of secukinumab in PsA and the MEASURE trials of the same drug in AS, making the data look less robust through this stringent trial design.[36,37]

When examining results, it is also useful to look at when end points were measured. Some trials are ended early for ethical reasons (one treatment has been shown to be so much better than the other that it is unethical to keep patients on the inferior treatment), but it is also possible to publish positive outcomes at interim time points, which may not reflect final study outcomes. This occurred in the Celecoxib Long-term Arthritis Safety Study (CLASS) of celecoxib versus traditional nonsteroidal anti-inflammatory drugs (NSAIDs), with positive results at 6 months being

Results

- ☐ Were all the enrolled patients included in the results (ITT analysis)?
- ☐ Were reasons given for patients who withdrew from the trial?
- ☐ Were dropout patients' results treated as if they were nonresponders?
- ☐ Were results provided for all the trial's specified end points?
- ☐ Were results provided for all the measured time points?

*The more questions you can answer with a "yes," the better the quality of the trial and its reporting.

published, whereas the results at the 12 months end point of the trial were negative.[38] Look back at the trial protocol to see whether results are being provided for all the time points originally planned, as well as for all the end points listed in the protocol.

Interpreting Results.

The ways in which data are described affect the way they are perceived. For example, it has been shown that physicians are more likely to use a therapy if its trial results are presented as a relative risk reduction (drug A reduced the risk by 40% more than drug B) rather than an absolute risk reduction (drug A reduced the risk from 10% to 5.8% while drug B reduced it from 10% to 7%) or number needed to treat (NNT; treating 83 patients with drug A instead of drug B would prevent one event).[39]

Data presentation. There are many ways to show data visually in order to make it easier for the reader to grasp. Kaplan-Meier survival curves are frequently seen in cardiology and oncology trial papers, but less so in rheumatology articles, which tend to use line graphs to demonstrate changes in outcome measures over time. Line graphs and bar graphs can be manipulated, however, most frequently by not including the entire y-axis, which can make an outcomes difference look much larger than it is.

Forest plots (Figure 2) are less common but are especially good at showing efficacy results for either a range of end points or the same end point in several subgroups (or several studies in the case of a meta-analysis). A single line is used to show each result, with a central box representing the mean effect estimate. In meta-analysis plots, the area of the box may vary to show the weight given to each study. The width of the line to either side of the box shows the confidence intervals (CIs) for that result. If they cross the vertical midline, which can represent a relative risk of 1 or a difference between groups of 0, the result is not considered statistically significant, since that means that the true result could lie on either side of the line and thus could favour either side.

Statistics. It has been standard practice for many years to use *p* values to calculate whether the results in a treatment group are statistically significantly different from those of a comparator group. In recent years, however, *p* values have come under scrutiny since they depend on not only the data but also the statistical method used and the assumptions made.[41] In addition, *p* values are often misconstrued as representing the probability of the null hypothesis being true (i.e., a *p* value of 0.04 means that there is only a 4% chance that the null hypothesis is true), rather than the probability of these results occurring if the null hypothesis were true (i.e., if there were no difference between the treatment groups, a *p* value of 0.04 means there would be only a 4% chance of getting these results by chance alone).

Another disadvantage of *p* values is that if enough tests are done, some will be positive through chance. A trial design with a large number of end points may be a sign that the researchers are hoping that at least one end point will prove to be statistically significant by the law of averages.

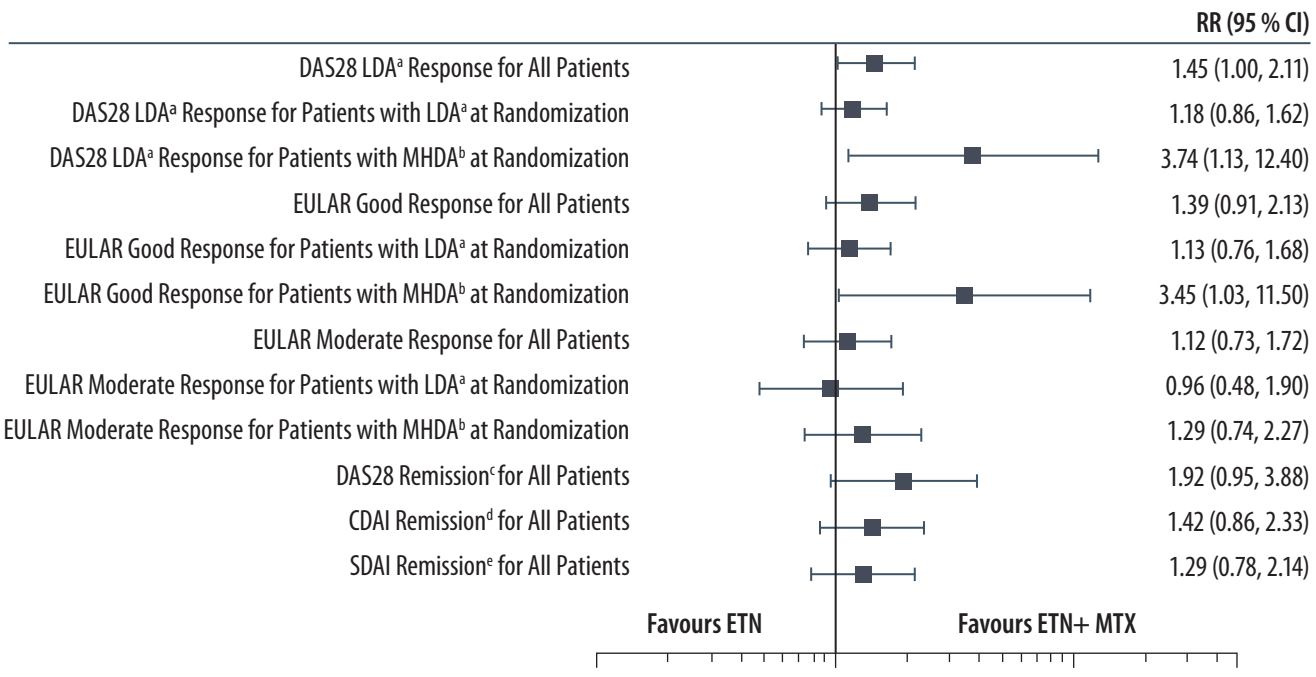
Some journals now prefer[9] that statistical significance be expressed through confidence intervals (CIs), which indicate the random variation around a point estimate. Unlike *p* values, CI calculations produce an estimated point value and show the range of values for the population (not the sample alone) that could plausibly produce that value. Rather than simply rejecting or supporting a null hypothesis, CIs also provide information on the variability (precision) of the sample statistic and its probable relationship to the population from which the sample was drawn.[42]

Drawing conclusions: In the discussion section of a paper, it is not uncommon to find study authors theorizing about the potential implications of their results. While such hypothesizing can be thought-provoking, it can lead the reader toward conclusions that are not actually supported by the data in the paper. For example, the authors of a placebo-controlled trial paper may discuss their results in comparison with those of another placebo-controlled trial although the two trial designs may have been vastly different. Head-to-head trials are the only way to reliably compare two interventions.

Authors may also discuss the fact that all other published trials involving a specific agent have demonstrated positive effects. This may be an inaccurate assumption: since trials with positive results are more likely to be cited and published, particularly in higher impact journals, than those with negative results, investigators may feel pressure to publish only those papers or report only those end points that achieved statistical significance.[7,41,43]

Discussions about class effects often appear at the end of papers, since there is a tendency to assume that drugs with the same mechanism of action, or even those only described as being in the same class, will have similar effects. Class effects are difficult to characterize and there is no uniformly accepted definition. This makes it difficult to determine whether a class effect even exists for a set of drugs, before establishing whether a particular agent shares that effect. It has been suggested that rather than assuming a class effect, clinicians apply a hierarchy of evidence when making decisions about drugs within a supposed class (Table 2). In general, it is considered wiser to look for evidence for a specific drug's efficacy and safety in a specified condition, as regulatory agencies do.

Figure 2:
Example of a Forest Plot



CDAI = clinical disease activity index; DAS = disease activity score; ETN = etanercept; LDA = low disease activity; MHDA = moderate-to-high disease activity; MTX = methotrexate; RR = relative risk; SDAI = simplified disease activity index; [a]LDA = DAS28 < 3.2; [b]MHDA = DAS28 ≥ 3.2; [c]DAS28 Remission = DAS28 < 2.6; [d]CDAI Remission = CDAI ≤ 2.8; [e]SDAI Remission = SDAI ≤ 3.3

Figure 2. Example of a forest plot showing relative risk results for a number of end points in the Canadian Methotrexate and Etanercept Outcome Study.[40] Where the black box is on the left side of the midline, the result favours etanercept; where it is on the right side, it favours etanercept plus methotrexate. The midline here represents a relative risk of 1, meaning no effect was seen.

Table 2:

Levels of Evidence for Comparing the Efficacy of Drugs within the Same Class.*[44]

Level	Comparison	Study Patient	Outcomes	Threats to Validity
1	Within a head-to-head RCT	Identical (by definition)	Clinically important	• Failure to conceal randomization scheme • Failure to achieve complete follow-up • Failure to achieve double-blinding • Soundness of outcome assessment
2	Within a head-to-head RCT	Identical (by definition)	Validated surrogate	• Those of level 1 plus validity of surrogate outcome for clinically important outcomes
2	Across RCTs of different drug vs. placebo	Similar or different (in disease and risk factor status)	Clinically important or validated surrogate	• Those of level 1 plus differences between trials in: – Methodologic quality (adequacy of blinding, allocation concealment, etc) – End point definition – Compliance rates – Baseline risk of outcomes
3	Across subgroup analyses from RCTs of different drugs vs. placebo	Similar or different	Clinically important or surrogate	• Those of level 1 (plus or minus those of level 2) plus: – Multiple comparisons, post hoc data dredging – Underpowered subgroups – Misclassification into subgroups
3	Across RCTs of different drugs vs. placebo	Similar or different	Unvalidated surrogate	• Surrogate outcomes may not capture all of the effects (beneficial or hazardous) of a therapeutic agent
4	Between nonrandomized studies (observational studies and administrative database research)	Similar or different	Clinically important	• Confounding by indications, compliance, and/or calendar time • Unknown/unmeasured confounders • Measurement error • For outcome research: limited databases, coding systems not suitable for research

*Clinically important outcomes refer to long-term efficacy data, and the particular end points depend on the condition being treated. Surrogate outcomes are considered validated only when the relationship between the surrogate outcome and clinically important outcomes has been established in long-term randomized clinical trials.

Interpreting Results

- ☐ Were results expressed in absolute as well as relative terms?
- ☐ Were graph axes shown in full?
- ☐ Were confidence intervals used to demonstrate statistical significance?
- ☐ Are the differences consistent across other studies?
- ☐ Did the authors confine their conclusions to the drug(s) being tested and not over-extrapolate?
- ☐ Did the discussion section avoid making conclusions about other trials?
- ☐ Do the findings make biological sense?

*The more questions you can answer with a "yes," the better quality of the trial and its reporting.

Discussion/Summary

This article has attempted to discuss the many factors that determine whether the results of a clinical trial can be applied to the patients in one's own practice. This is not an exhaustive review and many articles have debated the details at length. However, it is hoped that we have provided—along with the accompanying checklist for trial quality—an introduction to practising rheumatologists for better evaluation of the trial reports that cross their desks.

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Glossary

Absolute difference: The difference in the size of an outcome between two groups. For example, if drug A reduces an outcome by 10 points and drug B reduces it by 15 points, the absolute difference is 5 points. Contrast relative difference.

Adjusted analysis: An analysis that accounts (by adjusting) for baseline differences in important patient characteristics.

Attrition: The loss of participants over the course of a study, also called loss to follow-up.

Baseline: The initial time point in a study, just before the participants begin to receive the intervention being tested.

Blinding: A trial design procedure in which one or more groups involved in the trial (such as patients, investigators, and outside reviewers) are unaware of which patients have received which interventions.

Case-control study: A study in which patients with a particular condition are "matched" with controls (the general population, patients with another condition, etc). Data are then compared between the two groups, looking for significant differences. Usually retrospective and frequently concerned with causes of disease, rather than treatment.

Censored: In studies where the outcome is the time to a particular event, a term describing the lack of data from participants whose outcome is unknown. For example, if a patient is known to be alive only up to a certain point, "survival time" is censored at that point.

Clinically significant: A description of an effect large enough to be of practical importance to patients and health care professionals.

Cohort study: A study in which groups of people are chosen based on their exposure to a specific agent or their development of a certain condition and their long-term health is followed. May be retrospective.

Confidence interval (CI): A measure of the uncertainty around the result of a statistical analysis. A 95% confidence interval (abbreviated 95% CI) means that if the study were repeatedly done with other groups from the same population, 95% of the confidence intervals from those studies would contain the true value. Wider confidence intervals (eg, 90%) indicate less precision.

Confidence limits: The upper and lower boundaries of a confidence interval.

Control arm/group: A group of study participants who resemble those receiving the intervention being tested but who do not receive that intervention.

Controlled trial: A type of clinical trial in which outcomes are compared to a standard called the control. The control may be another intervention (active control), a placebo (placebo control), or observations from an earlier trial (historical control).

Crossover design: A trial design in which groups of participants receive two or more interventions in a particular order. For example, in a two-by-two crossover design, one group receives drug A initially, then drug B during a later phase. The other group receives drug B initially, followed by drug A.

Double-blinding: A type of masking in which two groups, typically investigators and patients, are unaware of which patients have received which interventions.

Effect size: The difference between two outcomes divided by the standard deviation of the population involved. Effect size focuses on the size of the outcome difference rather than the size of the treatment groups.

Equivalence trial: A trial designed to determine whether the effects of two or more treatments differ by an amount that is clinically unimportant.

Experimental arm/group: The group of participants who receive the intervention that is the focus of the study.

Factorial design: A trial design in which multiple groups of participants receive one of multiple combinations of interventions. For example, a two-by-two factorial design involves four groups of participants. Each group might receive one of the following: drug A and drug B; drug A and a placebo; drug B and a placebo; or two placebos. In this example, all possible combinations of the two drugs and placebo are each studied in one group of participants.

Hazard ratio (HR): A ratio comparing two hazard rates (how long until an event occurs). A hazard ratio above 1 suggests that the group represented by the first number (usually the treatment group) has a higher likelihood of the event over a specified time period than the second group (usually the control group). Unlike odds ratios, which estimate the likelihood of a cumulative event, hazard ratios estimate the likelihood of an event at a specific time point.

Intent-to-treat (ITT) analysis: An analysis of a trial's results that includes the data from every participant randomized, even if not all of them received the treatment.

Interim analysis: A preplanned analysis that compares the arms of a trial before the trial's official end. This is done so that a trial can be stopped if the difference between arms is so great that the participants in the arm with the less effective intervention are being put at risk unnecessarily.

Loss to follow-up: See attrition.

Masking: See blinding.

Noninferiority trial: A one-sided version of an equivalence trial, designed to determine whether one treatment's effect is not worse than another's by a clinically important amount.

Null hypothesis: The hypothesis that there is no difference between two groups. Trials are done with the goal of disproving the null hypothesis and showing that a true difference exists.

Number needed to harm (NNH): The average number of people who must be exposed to a risk factor over a specific period in order for one person to be harmed by it.

Number needed to treat (NNT): The average number of people who must receive a treatment in order for one person to avoid a negative outcome.

Observational study: A clinical study in which participants are observed and assessed for outcomes but not assigned to specific interventions. Cohort and case-control studies, among other types, are observational.

Odds ratio (OR): The ratio of the odds of an event in one group (usually the treatment group) to the odds of that event in another group (usually the control group). An odds ratio above 1 suggests that the first group is more likely to experience the event, while an odds ratio below 1 suggests that they are less likely.

Open-label: Describes a clinical trial in which masking is not used and therefore all parties involved know which participants have been assigned which interventions.

p value: The probability (ranging from 0 to 1) that the result observed could have occurred by chance if there were no difference between the effects of the interventions in the trial arms.

Parallel design: A trial design in which two or more groups of participants receive different interventions over the same time period.

Phase I study: A study usually conducted with healthy volunteers to determine a drug's safety.

Phase II study: A study to gather preliminary effectiveness data in patients with a specified condition.

Phase III study: A study to gather more information about a drug's safety and effectiveness by studying different populations, dosages, and drug combinations.

Phase IV study: A study occurring after regulatory agencies have approved a drug for marketing to gather further information about a drug.

Primary end point: The outcome measure considered the most important for evaluating an intervention's effect.

Prospective study: A study in which participants are identified then followed over time to observe events. Contrast retrospective study.

Relative difference: The difference in the size of an outcome between two groups, taking their size into account. It is always expressed as a ratio or percentage, not in units. For example, if drug A reduces an outcome by 10 points and drug B reduces it by 15 points, the relative difference is 50% (drug B reduces the outcome by 50% more than drug A).

Retrospective study: A study in which events have occurred to the participants before they are identified as part of the trial.

Secondary end point: An outcome measure that is less important than the primary end point but is still of interest in evaluating an intervention's effect.

Sham intervention: A procedure or device made to be indistinguishable from the procedure or device being studied but that does not contain active processes or components.

Single-blinding: A type of masking in which one group of people involved in the trial (patients, investigators, or reviewers) is unaware of which patients have received which interventions.

Standard deviation (SD): The average difference between a set of observations and their mean value, which indicates the spread or dispersion of the observations.

Statistically significant: Unlikely to have occurred due to chance alone. Measured by statistical tests that calculate p values and confidence intervals, among other results.

Superiority trial: A trial designed to determine whether the effects of one intervention are greater than the effects of another. Contrast noninferiority trial.

Surrogate end points: Markers (often physiological or biochemical) that can be relatively easily measured and are used to predict or represent important clinical outcomes that would otherwise be hard to measure.

CRA 2016 Access to Medications Survey Results

Access to medications is a serious concern for many patients and their healthcare professionals. Challenges in accessing medications are not only frustrating, but can even be a matter of life and death.

For this issue's Joint Count survey, we asked CRA members to rate their major and minor frustrations related to accessing medications for their patients, and to tell us which specific medications were difficult to access.

According to the 129 respondents, the top four major obstacles and/or frustrations included the paper work involved (61%), appealing rejections (59%), approval wait times with public payers (40%), followed closely by staying on top of changing policies (39%); refer to Tables 1 and 2 for further details.

Other concerns related to drug access cited by respondents included: drugs for rare diseases; off-label uses; the lag time between approval of drugs in other countries and Canada; and the difficulties of access to medications for pediatric patients.

When asked to list specific medications that are challenging to access for their patients, an overwhelming majority of CRA members mentioned rituximab, apparently due to the number of conditions for which there is a lack of approved indication and/or randomized controlled trials (RCTs). With regard to rituximab for granulomatosis with polyangiitis (GPA), one respondent explained "Patients with severe disease cannot wait the length of time public funding approval takes. Even more frustrating is the unwillingness to cover rituximab for maintenance, despite good evidence it is superior to currently available therapies." Rituximab was also reported as difficult to access for a number of other conditions, including rheumatoid arthritis and lupus.

Many also stated that biologics as a class were difficult to access; specific biologics that were mentioned include tocilizumab, adalimumab, belimumab, canakinumab, and anakinra. Others reiterated that most drugs for orphan diseases and off-label uses were also challenging to access.

Indeed, difficulties in accessing medications are a major issue in healthcare. The CRA and Ontario Rheumatology Association established a first when they negotiated an understanding with private payers, through the Canadian Life and Health Insurance Association (CLHIA), of a common criteria for use of biologic agents in RA. The CRA Therapeutics Committee is keen to receive documentation of challenges that present themselves, in order to present real examples to the appropriate agencies.

Indeed, it will take collaboration on all sides to improve access and, ultimately, the quality of life for patients.

Table 1. **Top Five Major Obstacles and Frustrations**

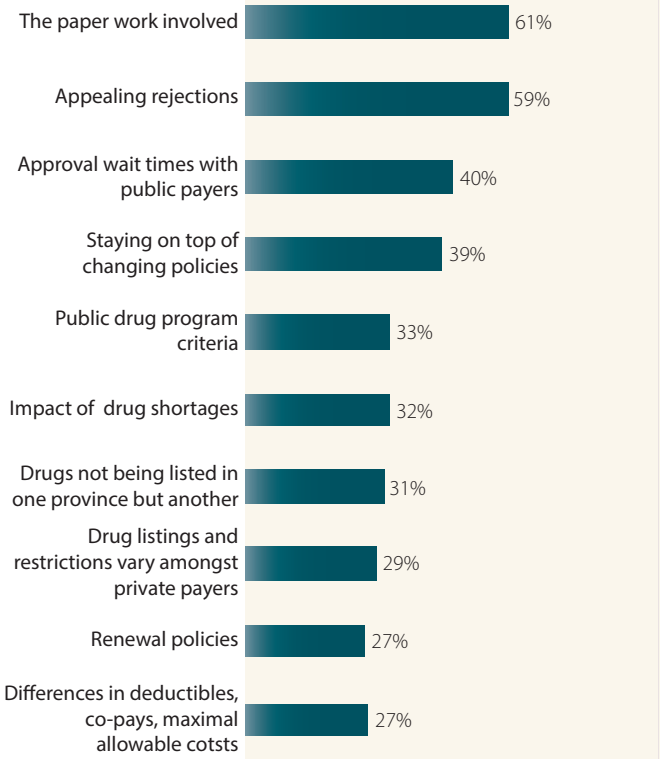
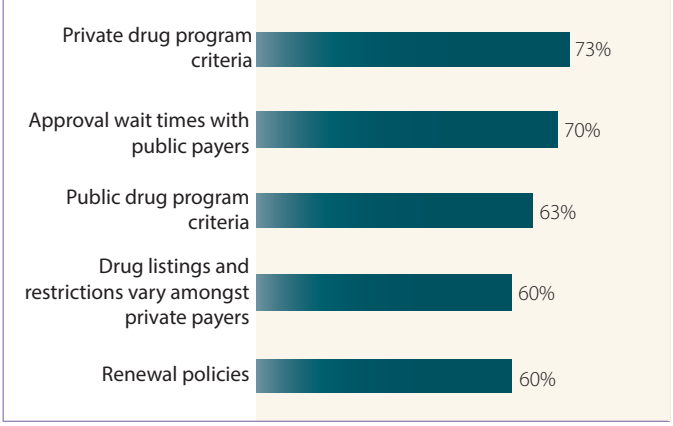
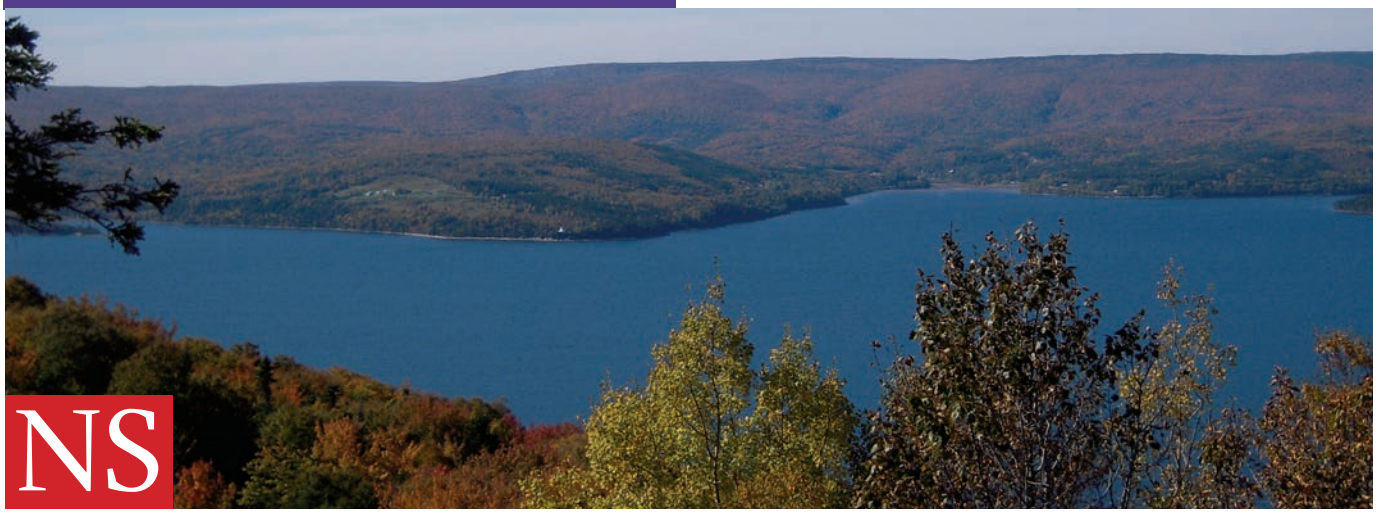


Table 2. **Top Five Minor Obstacles and Frustrations**





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News from Dr. Trudy Taylor

Dr. Evelyn Sutton was recently awarded the *Achievement in Medical Education Award* from the Department of Medicine at Dalhousie University, a nice way to finish off her term as Head of the Division of Rheumatology which ended in July. Dr. Volodko Bakowsky has taken over the helm as our new interim Division Head and will be sure to steer us on a successful course. In other news, there has been a significant amount of media coverage around Dr. Sutton's Collaborative Care clinic which she runs along with family physician, Dr. Sam Hickcox, and several physiotherapists and nurses in the Nova Scotia Rehabilitation and Arthritis Centre in Halifax. This coverage has been a great vehicle to keep the important issue of rheumatology care at the forefront of the minds of Nova Scotians.

Dr. Evelyn Sutton at Lake O'Hara.

Update from Dr. Juris Lazovskis

It has been 14 years since Dr. Juris Lazovskis drove a U-Haul from Minneapolis to Sydney, Nova Scotia, after finishing his fellowship at the University of Minnesota. What attracted him to and keeps him "holding the fort" as the sole rheumatologist on Cape Breton Island is the all-season splendour of the Cape Breton Highlands, the loyal patients and his team (pictured from left to right): office manager, Ms. Pamela Chant; research assistant, Ms. Carolyn Burns; and nurse, Ms. Lynn Vickers. "

Dr. Lazovskis and his team.

Update from Dr. Adam Huber

The Pediatric Rheumatology Team at the Izaak Walton Killam (IWK) Health Centre in Halifax, Nova Scotia includes four pediatric rheumatologists, two nurses, a physiotherapist, occupational therapist and social worker, along with a number of other outstanding support staff. We provide subspecialist pediatric rheumatology care to the three Maritime provinces and occasionally beyond.

IN MEMORIAM

It is with sadness that we share the news of the passing of Dr. Eva Arendt Racine, MDCM, FRCPC, on September 6, 2016, in Montreal, at age 97. Dr. Arendt Racine, a rheumatologist, received her certification from the Royal College in Internal Medicine in 1954. We wish to express our deepest condolences to her family.

The first and only anti-TNF indicated in nr-Ax SpA[1*†]

NOT ALL TYPES OF AXIAL SPA CAN BE SEEN WITH AN X-RAY[2]

Indication:
SIMPONI® is also indicated for:
- Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS) who have had an inadequate response to conventional therapies

Clinical use:
- No studies have been performed in pediatric patients
- Caution should be used when treating the elderly, as there is a higher incidence of infections in this population. There were no patients ≥65 years in the nr-Ax SpA study

Contraindications:
- Severe infections such as sepsis, tuberculosis and opportunistic infections
- Moderate or severe (NYHA class III/IV) congestive heart failure
- Patients who are hypersensitive to golimumab, or any other ingredient in the formulation or component of the container

Most serious warnings and precautions:
Infections:
- Serious infections leading to hospitalization or death, including sepsis, tuberculosis (TB), invasive fungal, and other opportunistic infections have been observed with the use of TNF antagonists including golimumab. Administration of SIMPONI® should be discontinued if a patient develops a serious infection or sepsis. Treatment with SIMPONI® should not be initiated in patients with active infections including chronic or localized infections.
- Physicians should exercise caution when considering the use of SIMPONI® in patients with a history of recurring or latent infections, including TB, or with underlying conditions, which may predispose patients to infections, who have resided in regions where TB and invasive fungal infections such as histoplasmosis, coccidioidomycosis, or blastomycosis are endemic.
- Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation) has been observed in patients receiving TNF-blocking agents, including golimumab. Tuberculosis may be due to reactivation of latent tuberculosis infection or to new infection.
- Before starting treatment with SIMPONI®, all patients should be evaluated for both active and latent tuberculosis.
- If latent tuberculosis is diagnosed, treatment for latent tuberculosis should be started with anti-tuberculosis therapy before initiation of SIMPONI®.
- Physicians should monitor patients receiving SIMPONI® for signs and symptoms of active tuberculosis, including patients who tested negative for latent tuberculosis infection.

Malignancy:
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which golimumab is a member.

Other relevant warnings and precautions:
- Geriatrics (65 years of age or older): Caution should be used in treating the elderly
- Risk of hepatitis B virus reactivation
- Risk of worsening or new onset of congestive heart failure
- Risk of infection with concurrent use of anakinra, abatacept or other biologics; concurrent use is not recommended
- Risk of hematologic reactions

For patients with severe active nr-Ax SpA* with objective signs of inflammation (OSI)

Choose SIMPONI®

NEW INDICATION

Treatment of adults with severe active non-radiographic axial spondyloarthritis (nr-Ax SpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence who have had an inadequate response to, or are intolerant of nonsteroidal anti-inflammatory drugs (NSAIDs).

- Risk of hypersensitivity reactions
- Risk of latex sensitivity
- Risk of clinical infections, including disseminated infections, with live vaccines and therapeutic infectious agents; concurrent use is not recommended
- Risk of autoimmunity
- May cause immunosuppression; may affect host defences against infections and malignancies
- Potential for medication errors
- Risk of new onset or exacerbation of CNS demyelinating disorders
- Risk of infection in peri-operative patients
- Adequate contraception must be used to prevent pregnancy in women of childbearing potential for at least 6 months after last treatment
- Not to breast-feed during and for at least 6 months after treatment with SIMPONI®
- Use with caution in patients with impaired hepatic function
- May have a minor influence on the ability to drive due to dizziness following administration

For more information

Please consult the Product Monograph at http://www.janssen.com/canada/products#prod-425 for important information relating to adverse reactions, drug interactions, and dosing information which has not been discussed in this piece.

The product monograph is also available by calling 1-800-387-8781.

* Non-radiographic axial spondyloarthritis
† Comparative clinical significance has not been established.

References: 1. SIMPONI® Product Monograph, Janssen Inc., August 8, 2016. **2.** Hochberg, MC, Silman, AJ, Smolen, JS, *et al.* (2015). Rheumatology. Philadelphia: Mosby/Elsevier.

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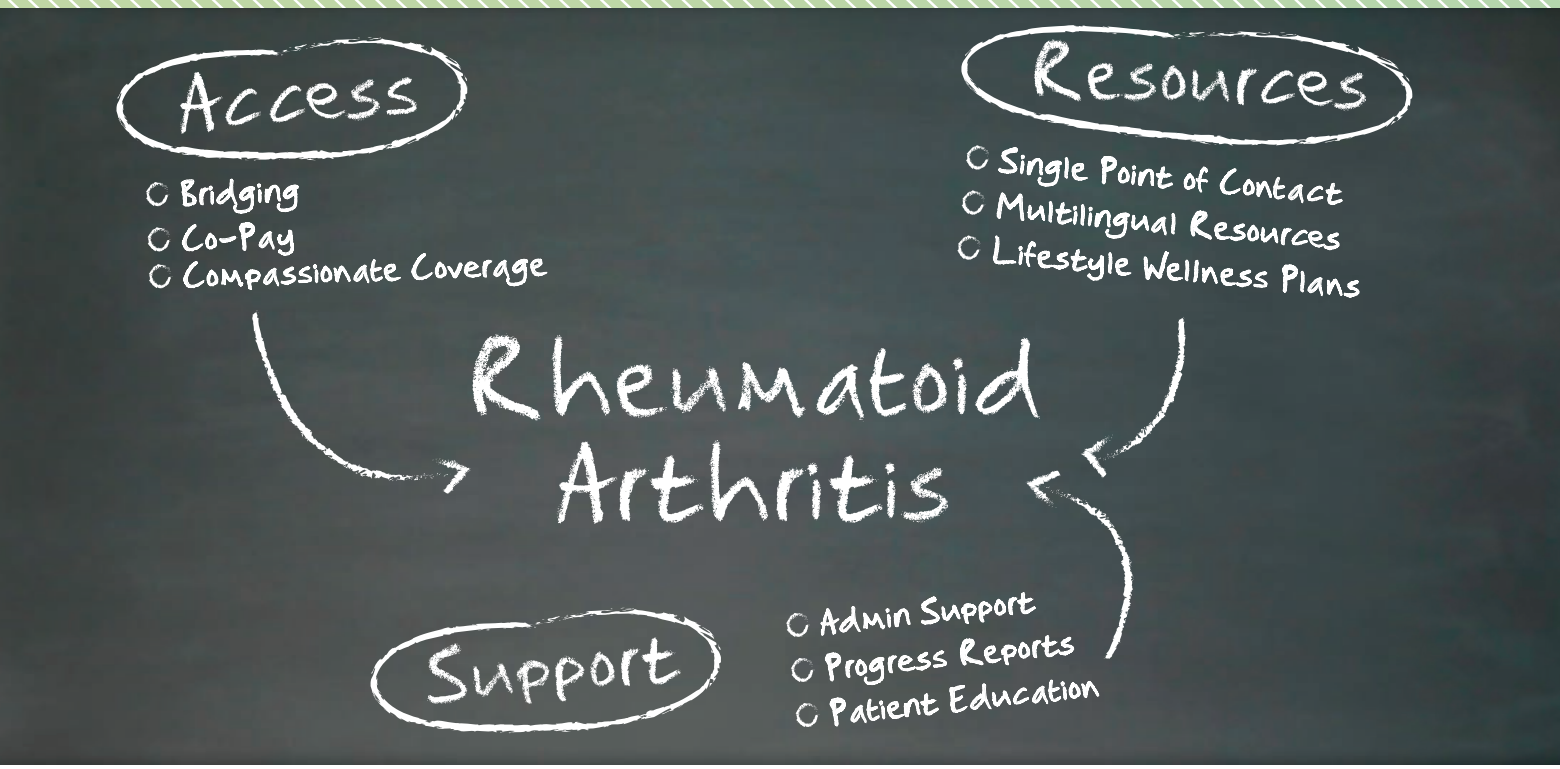

Designed to help support your RA patients

1-855-XEL-EXEL (1-855-935-3935)

XELJANZ (tofacitinib) in combination with methotrexate (MTX) is indicated for reducing the signs and symptoms of rheumatoid arthritis (RA) in adult patients with moderately-to-severely active RA who have had an inadequate response to MTX. In cases of intolerance to MTX, physicians may consider the use of XELJANZ as monotherapy.

Use of XELJANZ in combination with biological disease-modifying anti-rheumatic drugs (DMARDs) or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Please consult the product monograph at http://pfizer.ca/pm/en/XELJANZ.pdf for contraindications, warnings, precautions, adverse reactions, interactions, dosing information and conditions of clinical use. The product monograph is also available by calling us at 1-800-463-6001.