

THE NDB Research NEWSLETTER

News for Participants in the National Data Bank for Rheumatic Diseases January 2011

Notes from the Director

Frederick Wolfe, MD

How am I doing? How are we doing? It all depends.

If you have arthritis or some of the similar conditions we ask about, you know that these are chronic problems. Research doctors want to know how people with these conditions are doing – how well treatments work on *average*. But you and your doctor might be more interested in how *you, yourself*, are doing. A treatment might work well for most people, but not for you. This *group vs. individual* issue is the kind of problem that you see discussed in the media frequently when the FDA removes a drug from the market because it ‘doesn’t work.’ Yet some people who take the treatment have good results and are unhappy with the FDA decision.

Recently I received an email from an NDB participant who was concerned that an NDB study found that biologic treatment of RA didn’t work as well in NDB participants as it appeared to work in clinical trials. She had had a superb response to one of the biologics, and wondered whether what we found could be true. Her experience reflected the same group vs. individual problem: An individual may do better or worse than average.

But, how treatments work on average is a way to compare one treatment to the next.

In RA, one way to compare treatments is to study how well treatments lead to remission. Remission means the illness goes away, either permanently or temporarily. If a pharmaceutical company is testing a new treatment, then the percent of people who go into remission can be a good indication of how effective the treatment can be. And your doctor would certainly want to know if you are in remission – doing as well as possible. In some trials of biologic treatments remission has been noted in 50% of patients receiving the treatments. That’s an extraordinary

result. In effect it means that half the people are cured. Is that too good to be true? Yes it is.

Physicians have come up with a variety of definitions for remission, and recently a committee of researchers from the US/Canada and Europe has proposed a new “official” definition – the ACR/EULAR definition. You are in remission from your RA if you have no more than one swollen joint, no more than one tender joint, you rate the overall severity of your RA 10 or less on a 0-100 visual analog scale (VAS - take a look at severity question in the NDB questionnaire to get a better idea about the question), and your sedimentation rate blood test is low (below 30 for women and 20 for men). Before this definition became available there were a number of others.

We looked at remission using this definition in more than 1,400 people being treated by community rheumatologists (not in clinical trials or research settings). We found the

ACR/EULAR rate to be about 6%. That’s very different from the 50% quoted above. But in case you think we got it wrong, several researchers in different countries in Europe found the same

rate as we did. How could it be that there are such great differences? Well, it all depends on how you define remission. We found that when we tested with the widely used DAS criteria (Disease Activity Score) the remission rate was 27%, 4-5 times greater. More than that, the ACR/EULAR criteria agreed with the DAS criteria in only 20% of cases. And when doctors were asked about remission they also agreed with the ACR/EULAR criteria in just 20% of the cases.

You might ask, with such discrepancy, does assessing remission make sense? Yes. We need an official definition to help understand how people with RA are doing. But remission criteria and how *you* are doing are not necessarily the same thing.

“...how treatments work on average is a way to compare one treatment to the next.”

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Notes from the Director — continued

One of the problems with the ACR/EULAR assessment is your overall assessment of the severity of your RA. If you have pain in your back or difficulty moving because of damage to a joint, you may rate your overall severity as more than is allowed by the new criteria, even though your RA may be completely inactive. What kind of definition allows this type of contradiction? A definition that considers "groups of patients" rather than one patient. When assessing groups of patients, an average score of how they are doing is good enough because it doesn't matter if there are a few mistakes. But it would be wrong to apply this definition to an individual person with RA. Insurance companies often make this mistake as they try to assess whether a drug works and should be continued.

We at the NDB are constantly working on the problem of determining how well people with rheumatic diseases are doing. We have developed several fibromyalgia scales now in wide use to assess severity. Some of the scales are just for groups, but the newest ones that are included in the Diagnostic Criteria for Fibromyalgia can be used in individuals. We also aided in development of scales for Lupus over the last two years. As always, thanks for your help and participation. You, the group of individuals, make it possible.

NDB welcomes AIR patients!

This past summer the NDB and the Arthritis Foundation teamed up to create the new research study called AIR (Arthritis Internet Registry). Patients in AIR fill out questionnaires every 6 months along with everyone in the NDB, but in addition they're being asked to donate their blood. While we continue to see how all forms of arthritis are affected by different treatments, we're hoping to find out if there are clues in the blood that would tell physicians which drugs would work best the first time. We've just started this project along with researchers at Harvard Medical School and Quest Diagnostics. As we get more participants and questionnaires, expect to hear more about ways "biomarkers" in our blood can help.

About your medications

When listing your medications in the questionnaire, please include **everything** you take, even if they are not for your rheumatic disease. This means blood pressure meds, aspirin, pain killers, vitamins, supplements, etc. Even if they weren't prescribed or suggested by your doctor, and even if you take them only as needed, we want to know. Thank you.

Our website for rheumatology questions, RheumMD.org

On RheumMD.org we've brought together more than 20 volunteer experts to answer your questions about any rheumatic condition. You can also search existing questions and engage the doctors in discussions about the answers.



Here are some questions we've had on the site lately:

- How safe is prednisone if you have a history of glaucoma and cataracts?
- How does a TENS unit help fibromyalgia?
- What effects do RA medications have on healing fractures?

There are many more questions, and we invite you to ask your own at RheumMD.org.



Greetings from the NDB Staff

LATEST RESEARCH

Bias in clinical trials

Clinical trials test new medications in very small groups of people, evaluating their effectiveness and safety so they can be released to the market for broad use. People in clinical trials often report better improvements from the medications being tested than is reported by similar people not in clinical trials after the medications become widely available. The difference is important because the cost effectiveness of the medication can be greatly exaggerated during the trial, giving it an undeserved benefit in the marketplace. People may end up wasting limited financial resources and precious time taking new medicines that just aren't as great as they claim to be.

One interesting cause of inflated clinical trial results is the so-called Hawthorne effect. This effect was originally noticed in an industrial setting when workers who were singled out and made to feel important increased their productivity. The definition has been expanded to treatment response in medical settings. In a clinical trial, the Hawthorne effect may be defined as extra improvement caused by increased attention to participants during the clinical trial.

To test the Hawthorne effect we studied 264 RA patients who completed a commercially sponsored trial of a Food and Drug Administration approved RA

treatment. We evaluated changes in patient functionality, pain, overall health, and fatigue during three periods: at the start of the trial, at the end of the trial, and 8 months after the close of the trial. Patients were receiving the same treatment the entire time.

We found that from 23% to almost half of the benefits seen in the trial had disappeared 8 months after the end of the trial. The disappearing benefits can be attributed to the Hawthorne effect. Our results suggest that independent follow-up studies, removed from the trial assessment, can and should be used to estimate real-world improvement in new medications.

Progress of fibromyalgia

Fibromyalgia (FM) is a chronic condition for which treatment is frequently ineffective. But in a 2010 study of FM, 25% of patients in the study improved so much that they were not considered to have FM at the study's end. Other studies have also reported various degrees of improvement.

How do such improvements affect treatment? We looked at the question of symptom variability in 1,555 NDB participants over several years to determine the course of the condition.

People with FM often switch between having and not having FM based on their symptoms, and they have a wide variation in types and severity of symptoms. This makes it hard to give a useful and definite diagnosis of FM in some cases. Symptom severity, as opposed to an on-or-off diagnosis, appears to be more helpful when treating FM. Careful evaluation of the change in symptoms could reduce unnecessary treatment and side-effects when treating FM with powerful drugs.

Urinary tract infections

The NDB questionnaires ask a lot of questions about infections. We do this because when medications suppress the immune system, which is involved in the damage done by auto-immune diseases, infections can more easily take hold.

Looking at more than 100,000 questionnaires completed by more than 17,000 NDB participants with RA who reported urinary tract infections (UTI), we found a slightly increased risk of UTIs. 11.4% of women and 3.3% of men had UTIs. Only .39% of these infections required hospitalization or intravenous antibiotic treatment. Prednisone use or diabetes increased the risk of UTI, but biologic medications had no effect.

FOR MORE INFORMATION OR TO PARTICIPATE

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Please call 1-800-323-5871 ext. 140
or email info@arthritis-research.org

NDB Staff profile: Janice Anderson

One of the NDB's many wonderful employees, Janice Anderson, will retire this year. We thought the occasion was a good reason for everyone to meet her.

In her current role at the NDB, Director of Outcomes Assessment, Janice keeps things running smoothly, organizing the thousands of paper and online questionnaires that constantly arrive at the office, and the staff who process them. You may have talked to her if you needed help or had a mix up with your questionnaire.

Janice started at the NDB after using her biology training as a teacher for 26 years teaching science to students in junior high school up to community college. Her first NDB assignment was intended to be short-term, but now she looks back on more than 19 years in arthritis research.

The changes over the years have been numerous, especially in the growth of the NDB and the technology we use. Janice explained, "When I arrived, the two or three of us involved did a little bit of everything. We printed and mailed questionnaires, coded each page manually and called participants with questions. Today, mailing, coding and phoning are all done by different people and questionnaires, whether completed on paper or electronically online, are read by people sitting at computers."

Her favorite part of the job is seeing the final reports of projects, whether they described a new relationship, confirmed the existence of a side effect, or acknowledged the safety of a new drug, and knowing that she was part of making that news.

Janice's retirement plans sound more relaxing, however. "I'll be moving to

an old family home in Nebraska, where I can refurbish the gardens established by my grandmother, read the huge stack of books I always intended to get to someday, and volunteer and travel as opportunities arise," she said.

Janice often gives exit interviews to NDB study participants who need or want to leave the study. Because NDB data depends on people staying in the study, I asked her for her best pitch for them to stay in. Her answer contained a short history of arthritis treatment:

We have a group of about 20 participants who have completed questionnaires each 6 months for almost 30 years. They've reported to me how their initial treatment was mostly aspirin because there was little else available. Then along came methotrexate and it was the new miracle drug, but the thought of side effects was scary. Now it's the old standby and a plethora of new drugs for arthritis and fibromyalgia are on the market. These people are proud to have been a part of the history that studied their effectiveness.

Participants coming on board now need to realize they are closer to effective treatment, maybe even a cure, than anyone has ever been before. With thousands of people reporting their experiences, the steps will be taken faster than would be possible without them. There is a good chance that participants or their family members will have arthritis or fibromyalgia 30 years from now, and wouldn't they like to spend some time with questionnaires now if they could improve treatment for their loved ones?

We hope you agree that the answer is "yes."



Janice Anderson, NDB Director of Outcomes Assessment, will retire this year

Janice concluded the interview, explaining that her work at the NDB has been enjoyable and rewarding, and the decision to retire has been difficult. "Working with the researchers and the staff here has been a real pleasure and I'll continue to watch for news of their efforts."

Reminders

While working on your questionnaire, if you have ANY questions about the questionnaire, please contact us right away by email or phone. These might be about technical difficulties or how to interpret a question. If you put your immediate questions in the comments section we probably won't see it in time to answer.

Please use the comments section for any information you think we should have that isn't covered in the questionnaire. This could be about a change in medication that needs explanation or information about other considerations of your condition that you think we need to know. You may also ask general questions that don't require an immediate answer.

Welcome New Participants!

Everyone who works for the NDB and all of the doctors and researchers who benefit from our research are extremely grateful for the dedication of you, the participants, to helping this project. Many of you have been with us for several years or more. But every 6 months we are also glad to see many new people join us. Here is a quick primer on the NDB for the new and a refresher for the old timers.

The NDB is a non-profit organization that performs research in rheumatoid arthritis, osteoarthritis, fibromyalgia, lupus and other rheumatic diseases. The research is designed to improve the treatment and outcomes of these conditions.

The NDB is an independent organization that conducts its own research without influence from pharmaceutical, insurance, financial or other outside interests. Our research is so well respected that we are often hired to provide independent drug safety verification to the government.

Your personal information will always remain private. We do not sell or share any identifying information about NDB participants. Before we work with researchers or collaborate

with other research groups we remove any of your answers that could be used to identify you.

Nearly all of our research is available for you to read on our website.

We are glad to answer your general questions about rheumatic diseases and treatments, but we are not able to give personal medical advice.

NDB research is different in an important way: Participants report on themselves; data is not collected by doctors or medical staff. With patient-reported data, researchers get a perspective that short, small clinical trials cannot provide. Our long-term study offers a much broader view of treatment and results. Clinical trials are good at identifying common side effects, but rare or subtle problems, or problems that take longer to develop, are better detected by studies like the NDB. The same is true of long-term effectiveness of a treatment.

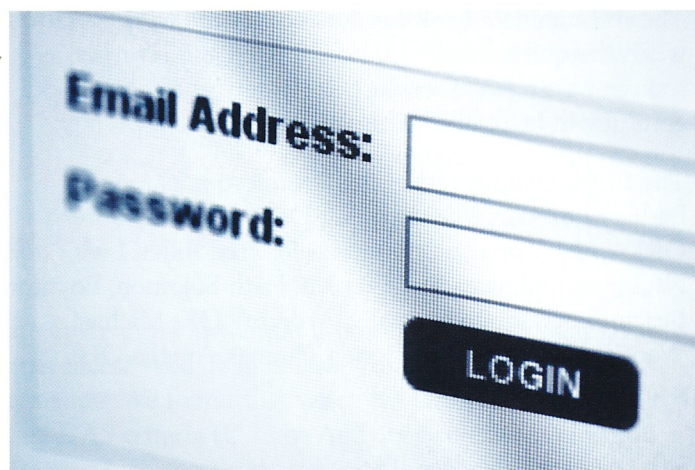
So, welcome to the NDB, or thanks again for your continuing participation! If you ever have any questions or need help with your questionnaire, feel free to contact us.

NDB Website changes

Over the next six months we will be introducing some changes to the NDB website. We're going to make it easier to get your online questionnaire, monitor your progress as you work on it, and let you update your contact information at any time. We will ask a small group of you to help us test this before we open it up to everyone for the July questionnaire.

Here are the main things to look for:

- Instead of a complicated link by email or having to ask us for your "Patkey", you will visit the website and sign in with your email address and a password of your choosing. You will be able to update your contact information online whenever you want, instead of contacting our office during our office hours.
- Eventually you will be able to record important medical events and medication changes whenever you want, instead of trying to remember them six months later when you fill out the questionnaire.



- You will need to choose a password and confirm your email address the first time you visit the site. This is an added convenience feature that also protects your privacy.

We will contact you by email when the changes are ready. Please let us know of any ideas you have for improving the website.

Questionnaire Changes

Like most times, we've dropped a few questions and added a few. The five new ones will look very similar to another set of questions. The large international group of researchers who designed the originals has updated them, and we have to ask, just this once, both versions before we can drop the older one.

WebQuest users will see a new type of question, Computer Adaptive Testing (CAT), in which you will be asked one question at a time. After each response, the computer will know which question to ask next to reach a final score much faster. Our goal is to be able to know more about your health in 4-5 CAT questions that we hope can replace up to 36 static questions. This is part of a nation-wide effort to build more efficient questionnaires. Rest assured that we are always trying to find ways to reduce the number of questions we ask.

Important Information about Email

For patients using WebQuest, email is our primary method of getting in touch with you. Even if you're not using WebQuest, we'd like to be able to send you important information by email.

We cannot emphasize enough how important it is for you to let us know whenever you change your email address. To update your email address go to our website and look in the participant's links, or call us.

Here's a VERY IMPORTANT step you can take to make sure our email gets to you: Add us to your email address book. Our address is webquest@arthritis-research.org. This will ensure that our mail makes it through the spam blockers. You will need to do this every time you change your email address. Thank you!



Join Us On Facebook

You can find us on Facebook as "National Data Bank for Rheumatic Diseases." We will try to keep you up to date with any news items that occur between questionnaires. You can also connect with other participants and NDB staff who have joined our group.

Lottery Winners!

The research data bank can best contribute to research when the questionnaires are completed and returned as soon as possible. We conduct the lottery as a token of our gratitude in help with rheumatology research.

The \$1,000 winners from the last questionnaire were Barbara Boisjolie, Maricopa AZ; Doris Clausen, Dorena OR. Winning smaller amounts were Fred Billet, Livingston NJ; Bonnie Johnson, Bay City MI; Faith Solomon, Boynton Beach FL; Clorinda Gonzales, Ardmore OK; Michael Woods, Watertown NY; Donna Thomas, Amelia OH. Congratulations to all!

WebQuest

WebQuest is the online version questionnaire. The questions are the same as the ones on the paper questionnaire. People who are comfortable using computers should find it easier than the paper version. If you would like to try it, follow the links from our home page, www.arthritis-research.org and make the request, or send us an email at webquest@arthritis-research.org.

Support rheumatic disease research with a financial donation

As a non-profit project conducting ongoing research to improve conditions for people with arthritis, fibromyalgia, lupus and other conditions, the NDB is an organization with ongoing financial needs.

If you would like to make a tax-deductible monetary donation to the NDB to help support this research, we would be very appreciative of your support.

If you would like to make your donation in memory of or in honor of someone please let us know. We will send a card to the person of your choice to acknowledge your gift.

Donations should be payable to:

The Arthritis Research Center Foundation Inc.
and sent to:

The Arthritis Research Center Foundation Inc.
1035 N Emporia Ste 288
Wichita, KS 67214

For more information please contact Rebecca Schumacher at 1-800-323-5871.

Thank you very much for considering a donation to support this important research.