

Biologic Therapies- The Changing Landscape of the Management of Rheumatoid Arthritis

May 29, 2014



Established in 1959, 321 Canada Gairdner International Awards have been given to scientists from 15 countries; of these recipients, 82 have subsequently won the Nobel Prize.

- *Great research has no borders. The Gairdners ...Canada's only major international scientific prize, inspire medical research, present and future. They are ours, but they belong to the world.*

Globe and Mail, Editorial October 2009

"For the discovery of anti-TNF therapy for the treatment of rheumatoid arthritis and other inflammatory diseases"

Sir Ravinder Maini



"For the discovery of anti-TNF therapy for the treatment of rheumatoid arthritis and other inflammatory diseases"

- Sir Marc Feldman



The Impact

- They discovered the first treatment for RA, using monoclonal antibodies which are genetically engineered natural defense molecules. Not only was this a novel treatment, but it was the first demonstration of the efficacy of a biological therapy for a chronic autoimmune disease and led to the recognition by the pharmaceutical industry that biological drugs are a viable class of therapeutic agents that can compete with traditional chemical drugs. The effective results have not only transformed the treatment for patients, but have led to other successful anti-TNF treatments, and encouraged much further work using antibodies for treatment.

The Past







Canadian Medical Association Journal

January 1963

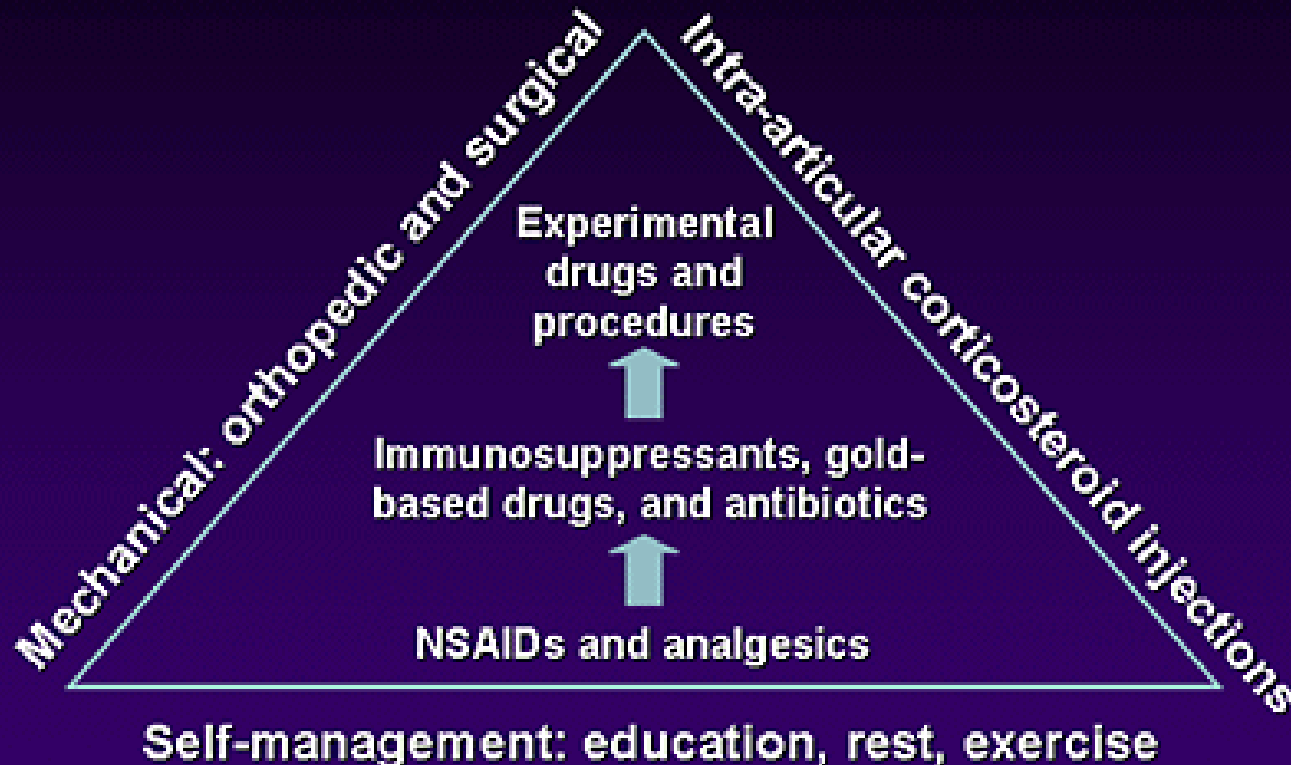
- 1000 RA patients treated at the Royal Devonshire Rehab Hospital in Buxton, England from 1953-1958
- Most patients substantially disabled bed bound, 84% moderately to severely disabled
- 60% between the ages of 40-60 years
- Admitted for “relatively short” stay- 3 months

- Work resettlement issues- patients systemically unwell, relapse rate high, effects small and large joints
- Upon discharge 33% fit for work, and at follow up > 50% disabled
- Conclusion: “Having returned to work in a single year would cover the cost of treatment of all RA patients treated in our rehab unit”

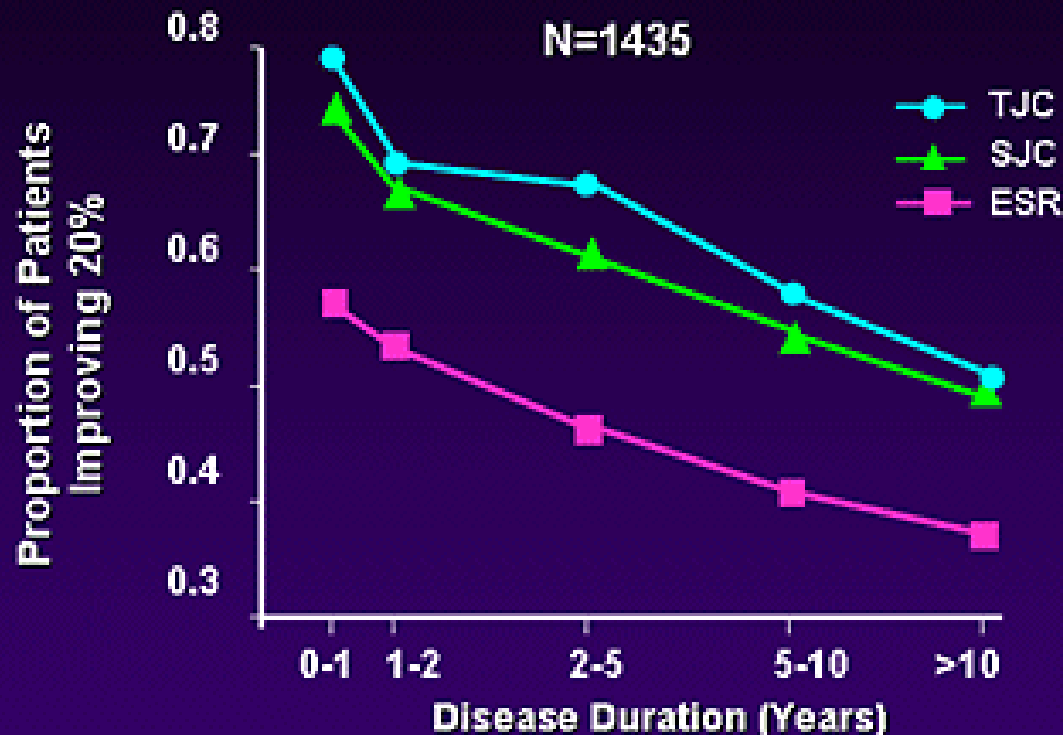
What has changed? What is the present

- Early recognition and early treatment of RA
- Treat to target
- Use of combination DMARDs
- Effective new therapies- biologics!

Traditional Treatment Pyramid for RA



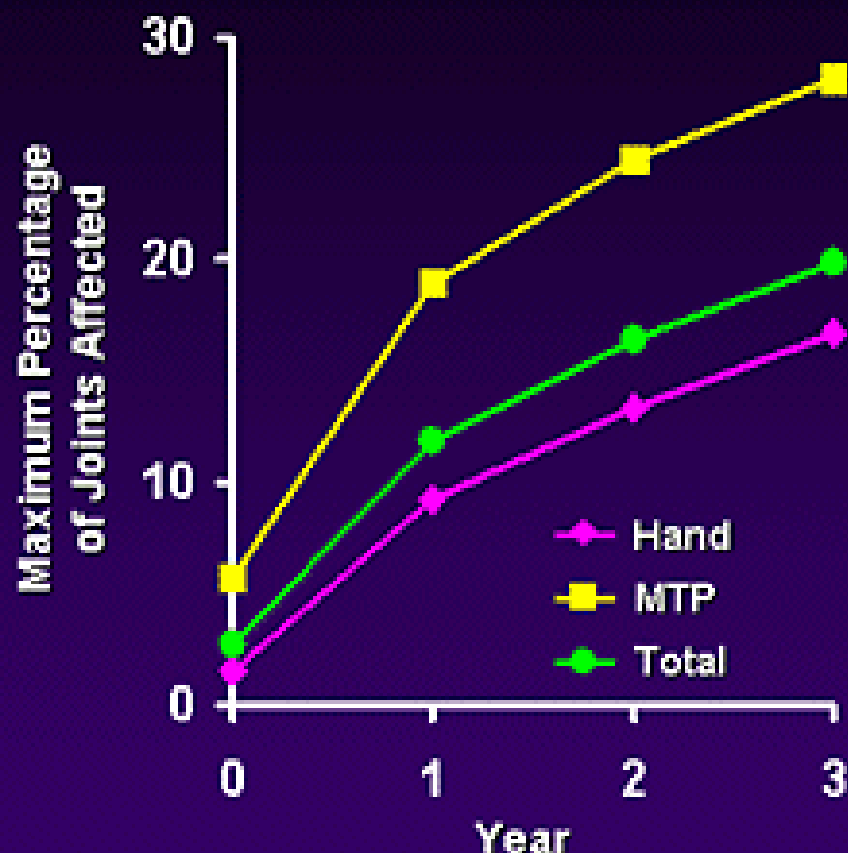
Disease Duration Predicts Response to Treatment in RA



*Primary trial data analyzed from 14 randomized, controlled trials: 11 MTX, CyA + MTX, COBRA, and Preserba.

Anderson JJ, et al. *Arthritis Rheum.* 2000;43:22-29.

Joint Erosions Occur Early in RA



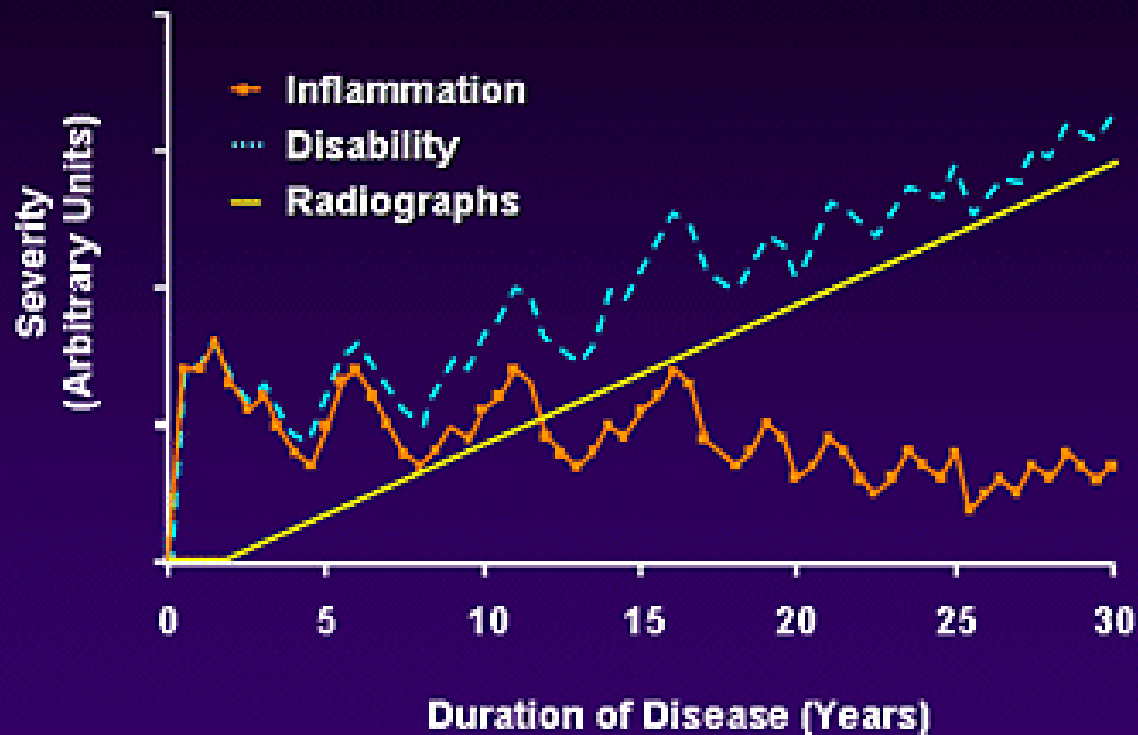
- Up to 93% of patients with <2 years of RA may have radiographic abnormalities
- Erosions can be detected by MRI within 4 months of RA onset
- Rate of progression is significantly more rapid in the first year than in the second and third years

van der Heijde DM, et al. *J Rheumatol*. 1995;22:1792-1796.

Fuchs HA, et al. *J Rheumatol*. 1989;16:585-591.

McQueen FM, et al. *Ann Rheum Dis*. 1996;57:350-356.

Course of RA Over 30 Years: Schematic Representation



Kirwan JR. *J Rheumatol.* 1999;26:720-725.

Treatment

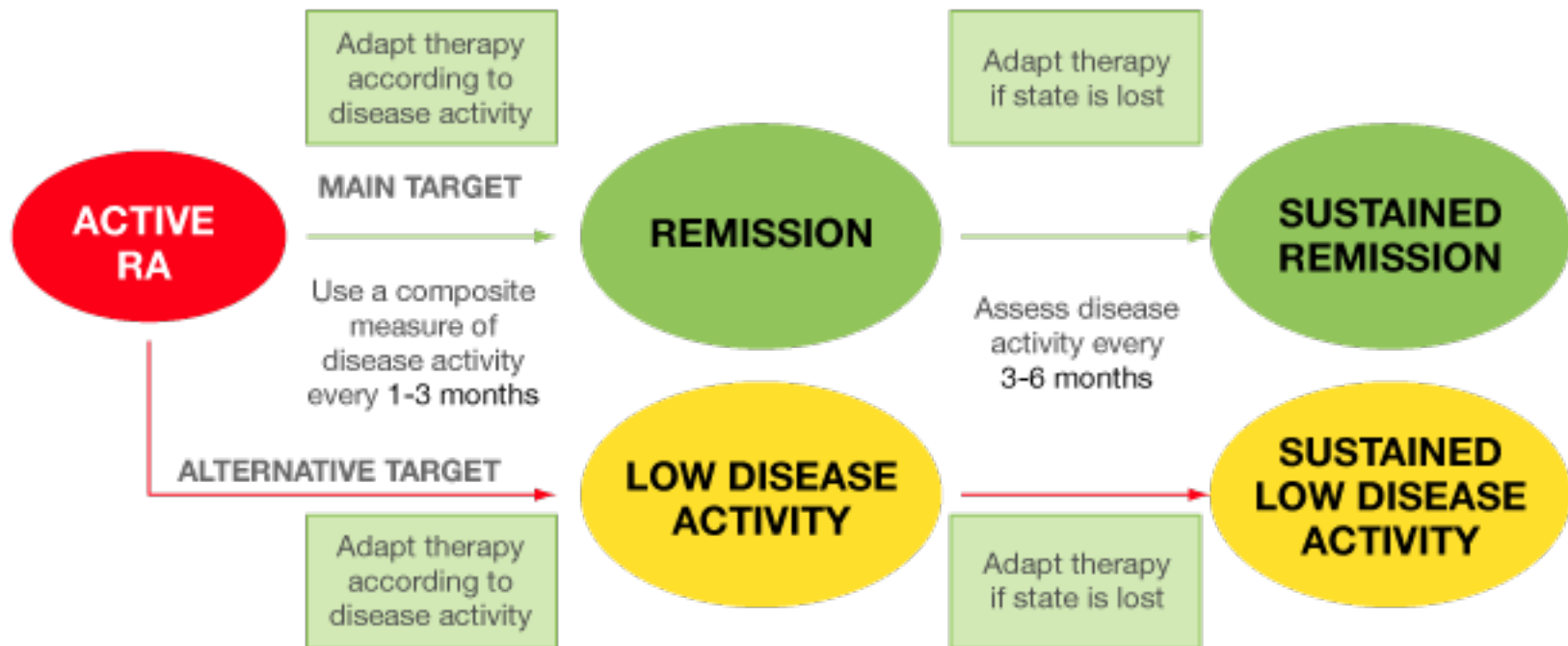
- Therapies for Active RA after Methotrexate Failure- N Engl J Med 2013; 369:307-318- 48 week double blind non inferiority trial of 253 patients demonstrating the non inferiority of triple therapy vs etanercept and MTX
- 27% at week 24 required a switch of therapy
- Swefot and TEAR trials also demonstrated efficacy of DMARDs in early disease

CATCH- Canadian Early Arthritis Cohort

- 19 sites in Canada, 1450 patients
- <50% clinical remission despite methotrexate, jrheum 2010
- Results of disease activity different at different sites with best results from sites using combination therapy and sc MTX : jrheum 2013

Treat to Target

- **Reference: 1.** Smolen JS, Aletaha D, Bijlsma JWJ, et al. Treating rheumatoid arthritis to target recommendations of an international task force. *Ann Rheum Dis.* 2010;69(4):631-637.



The Results

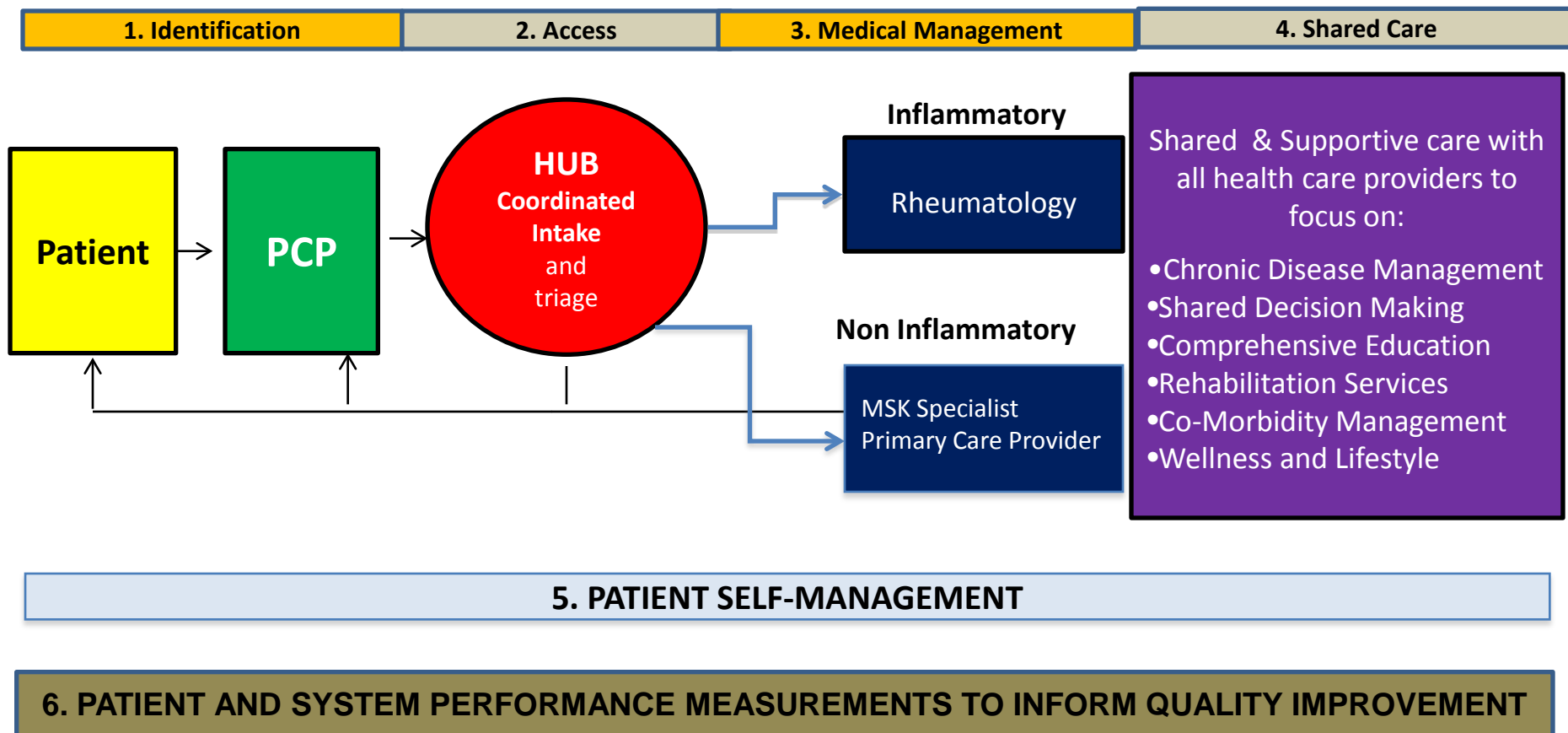
- 8 biologic therapies on the market in Canada with various mechanisms of action
- 60/40/20 rule, about 30% in clinical remission
- Few in patient beds in the country for patients with rheumatic diseases
- Orthopedic surgery almost eradicated in this population
- Decrease in cardiac disease and other comorbidities

Evolution of cost structures in rheumatoid arthritis over the past decade

- BMJ January 2014
- Cost increase of €4914 to €8206 in patients aged 18–64, and from €4100 to €6221 in those aged ≥ 65 , attributable to increasing prescription of biologic agents (18–64 years from 5.6% to 31.2%, ≥ 65 years from 2.8% to 19.2%).
- Decrease in hospitalization, disability and sick leave

- “Given the trend to earlier treatment initiation, improved treatment strategies with conventional DMARDs, including triple therapy and overall better outcomes, we do not expect further large cost increases for the treatment of RA in Germany in the next few years.”

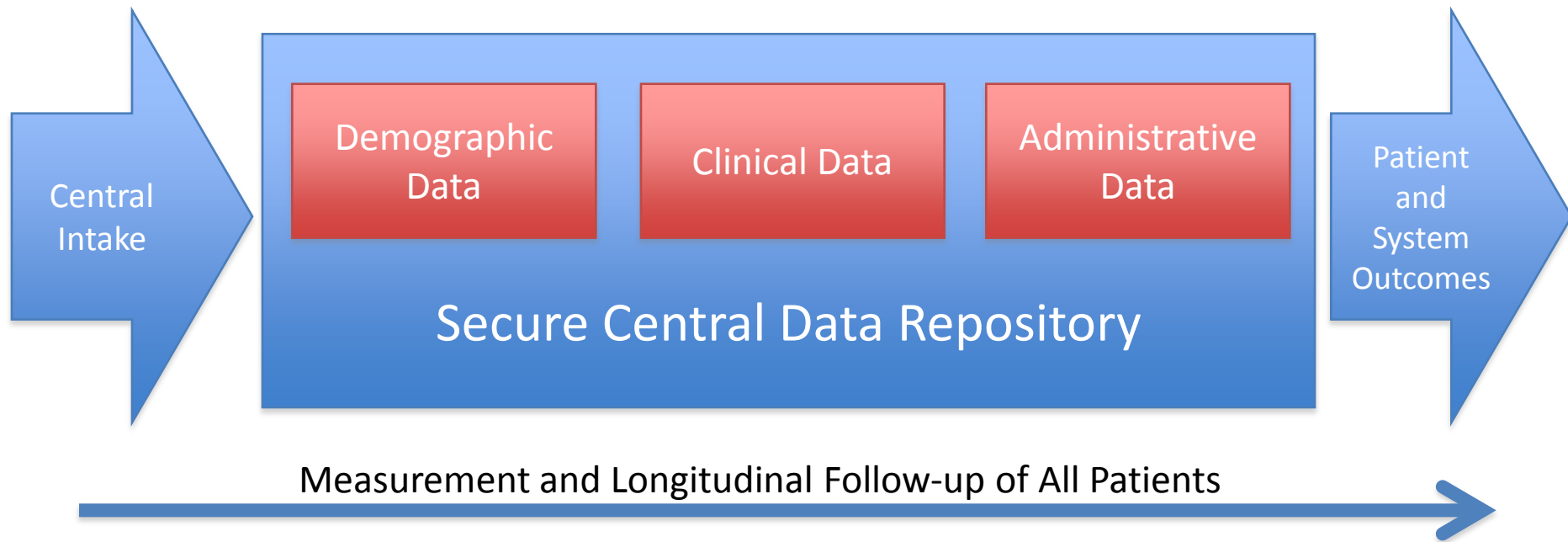
Inflammatory Arthritis MOC: Six Key Elements



The Future

- Subsequent entry biologics
- Small molecules
- New disease indications
- Personalized medicine

If we don't measure it, we don't know what we are doing!!



Thank You!



Emerging Themes in RA Management

