# Comparative effectiveness of three TNF inhibitors for rheumatoid arthritis:

## Quasi experiment with no large risk on confounding

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## Initiation of DREAM

- A registry of the use of TNF blocking agents in daily clinical practice was started on request of Dutch Health Care Institute (ZiNL)
- Objective: to determine the cost-effectiveness of these expensive 'new' drugs in daily clinical practice

## Comparative effectiveness (1)

- Three different TNF alpha inhibitors on the market/ in the pipeline
- Which one to prefer?
- RCT was not granted

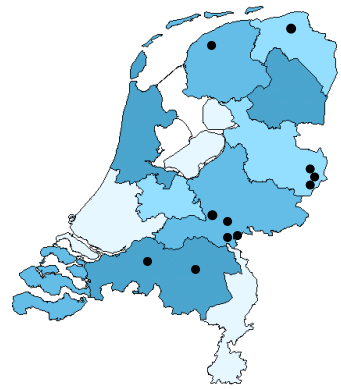


## Comparative effectiveness (2)

- Difference in availability of TNFi
- → Quasi experiment
- Comparable to instrumental variable analysis

## The DREAM study

- Inclusion of every RA patient that started with one of the TNF inhibitors since February 2003
- Collaboration between 11 hospitals in the Netherlands
- Regularly visits to assess medication use, effects and adverse events
- Clinical outcomes, patient reported outcomes; resource utilization



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# 707 with at least 1 year FU and fully accessible data (August 2007)

| | Adalimumab N=267 | Etanercept N=289 | Infliximab N=151 | p-value | Missing values (%) |
|---|---|---|---|---|---|
| % rheumatoid factor + | 81,0 | 71,1 | 77.7 | 0.022 | 1 |
| % female | 70.0 | 68.9 | 70.2 | 0.939 | 0 |
| % with ≥ one erosion | 71.7 | 65.3 | 72.7 | 0.157 | 1 |
| Age | 55,1 (12,6) | 54,6 (14,2) | 57,8 (13,4) | 0.05 | 0 |
| Disease duration (years) $ | 7.7 (2.7-13.6) | 6 (2.1-13.4) | 7.7 (2.7-14.1) | 0.356 | 1 |
| N previous DMARDs $ | 3 (2-4) | 3 (2-4.75) | 3 (2-5) | 0.385 | 0 |
| HAQ | 1,3 (0,7) | 1,4 (0,7) | 1,4(0,7) | 0.176 | 10 |
| DAS28 | 5,3 (1,3) | 5,5 (1,2) | 5,2 (1,3) | 0.059 | 4 |

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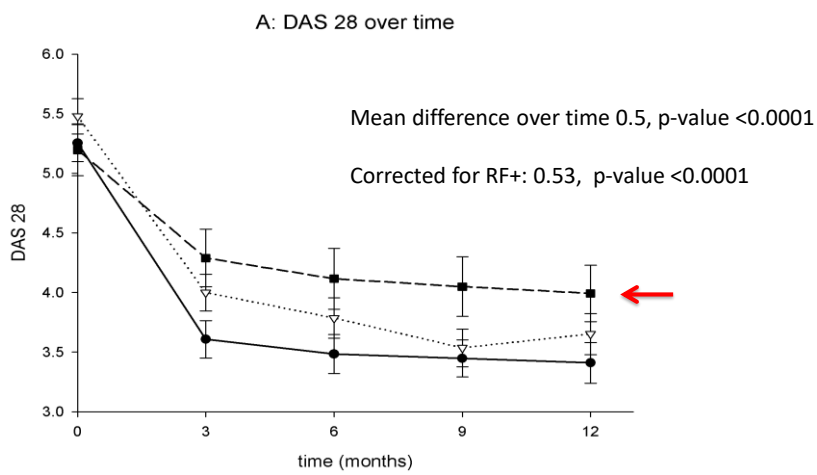
# Controlling for confounding

- Statistically significant differences, rheumatoid factor, age and DAS28 (outcome measures).
- Are the differences relevant?
  - Magnitude of the difference
  - association with the outcome
- Fitting propensity score failed because none of the factors predicted choice of treatment (is in line with results on previous slide)
- Linear mixed model for repeated measures, baseline DAS28 included by using random effect for patient and rheumatoid factor was included as a co-variat

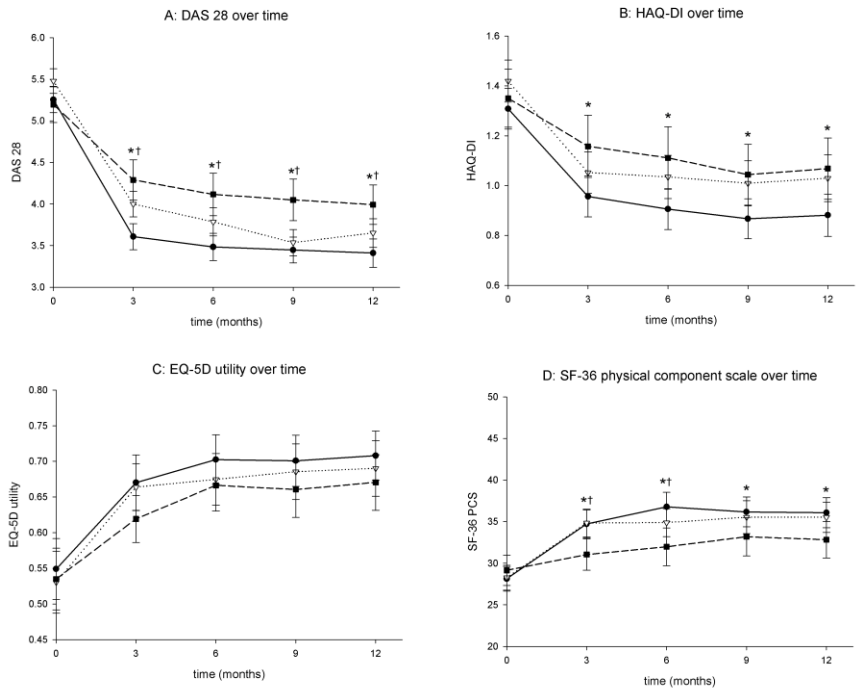


# Effectiveness: disease activity






Kievit et al, Ann.Rheum.Dis., 2008; 67(9):1229-34




# Conclusion concerning comparison

- One TNFi was less effective compared to the other two TNFi
- Effect was relatively large (0.6 = clinically relevant)
- Results were plausible (dose finding studies show the same results)
- Consistent with results from other observational studies
- In this case very little differences in baseline prognostic factors due to:
  - Availability issues
  - No expected difference in performance of the drugs

# Conclusion

- In the absence of head-to-head comparisons, a comparison using observational data is first best alternative if
  - Outcome is accurately measured (objective vs subjective)
  - Loss of follow-up is minimalized
  - Effect is large, consistent and biological plausible
  - Potential biases are corrected for sufficiently
  - Dose response relation