



Media Contact: **Bonny Senkbeil/Erin Latimer**  
Office – (404) 633-3777  
Newsroom – (619) 525-6204  
[bsenkbeil@rheumatology.org](mailto:bsenkbeil@rheumatology.org)  
[elatimer@rheumatology.org](mailto:elatimer@rheumatology.org)

### **TRIPLE DMARD THERAPY IS MORE COST-EFFECTIVE THAN METHOTREXATE MONOTHERAPY IN TREATING RHEUMATOID ARTHRITIS**

**SAN DIEGO** — Using a combination of three traditional disease-modifying antirheumatic drugs for treating recent-onset rheumatoid arthritis is not only more cost-effective, but results in better long-term worker productivity than a monotherapy approach using methotrexate, according to new research presented this week at the American College of Rheumatology Annual Meeting in San Diego.

[Rheumatoid arthritis](#) is a chronic disease that causes pain, stiffness, swelling, joint destruction leading to limitation in the motion and function of multiple joints. Though joints are the principal body parts affected by RA, inflammation can develop in other organs as well. An estimated 1.3 million Americans have RA, and the disease typically affects women twice as often as men.

Researchers in the Netherlands analyzed data on 281 patients with recent-onset RA who participated in a single-blinded, randomized clinical trial of RA therapies called the treatment in the Rotterdam Early Arthritis Cohort, or tREACH. The same group of researchers had proven that triple therapy of methotrexate, sulfasalazine and hydroxychloroquine was more effective at treating RA symptoms than methotrexate monotherapy, independent of corticosteroids. They examined the same set of data to find out how these therapies compared in cost-effectiveness.

“Sufficient data on efficient use of expensive drugs, especially biologic agents, are needed to be able to continue optimal rheumatic care in the future,” says Pascal de Jong, PhD; Department of Internal Medicine, Erasmus MC, and lead investigator of the study. “Therefore, we investigated the cost-effectiveness of different initial treatment regimens within our tREACH trial.”

Participants in the tREACH trial were randomly split into three groups, each given different induction therapy regimens. The first group of 91 patients received triple DMARD therapy, or 25mg of methotrexate per week, 2g of sulfasalazine per day, and 400mg of hydroxychloroquine per day, in addition to 120mg of intramuscular glucocorticoids once.

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## **TRIPLE DMARD THERAPY IS MORE COST-EFFECTIVE THAN METHOTREXATE 2**

The second group of 93 patients received the same triple DMARD therapy with a tapered dose of oral glucocorticoids starting at 15mg per day. The third group of 97 patients received 25mg of methotrexate per week with a similarly tapered dose of oral glucocorticoids, starting at 15mg per day. Participants were 68 percent female and their average duration of having RA symptoms was 166 days. At the beginning of the study, 267 (95 percent) of the participants fulfilled the 2010 ACR Criteria for RA, 216 (77 percent) tested positive for anti-citrullinated protein antibodies, and 48 (17 percent) showed evidence of joint erosions.

Participants were examined every three months to assess their progress, including measuring disease activity scores and collecting data from the Health Assessment Questionnaire. After 12 months of therapy, the researchers also analyzed X-ray progression. In addition, data on the patients' quality adjusted life years (called QALYs), and direct and indirect costs were evaluated. QALYs express the influence of disease burden on patient's health over time. Living in perfect health for one year corresponds with a QALY of 'one', on the other hand a QALY of 'zero' reflects death. Direct costs are the costs of treatment and medical consumption, and indirect costs are the costs incurred by loss of worker productivity, such as days of work missed due to sick leave and unemployment.

Both direct and indirect costs were higher for monotherapy patients compared to those who received triple DMARD therapy. The researchers concluded that the difference in costs was due to the monotherapy patients requiring 40 percent more biologic drug usage due to the monotherapy's inadequate control of disease activity. The triple therapy patients also reported less long-term sick leave time, less unemployment time and fewer contract hours than the monotherapy patients.

QALY scores were 0.75 for the first triple therapy group, 0.76 for the second triple therapy group and 0.73 for the monotherapy group. Total costs (direct and indirect) per QALY were €12,710 for the first triple therapy group, €10,371 for the second triple therapy group and €17,357 for the monotherapy group. There was no difference between the corticostereoids regimes.

Based on this data, the researchers concluded that triple DMARD therapy is more cost-effective, and results in greater long-term worker productivity, than methotrexate monotherapy independent of corticosteroids, in patients with early-onset RA.

**-MORE-**

### **TRIPLE DMARD THERAPY IS MORE COST-EFFECTIVE THAN METHOTREXATE 3**

“We recommend triple DMARD therapy over methotrexate monotherapy in newly diagnosed RA patients, because of lower costs per QALY and in addition better worker productivity when triple DMARD therapy is compared with methotrexate monotherapy,” says Dr. de Jong.

Patients should talk to their rheumatologists to determine their best course of treatment.

The American College of Rheumatology is an international professional medical society that represents more than 9,000 rheumatologists and rheumatology health professionals around the world. Its mission is to advance rheumatology. The ACR/ARHP Annual Meeting is the premier meeting in rheumatology. For more information about the meeting, visit <http://www.acrannualmeeting.org/> or join the conversation on Twitter by using the official hashtag: #ACR13

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*Editor’s Notes: Dr. de Jong will present this research during the ACR Annual Meeting at the San Diego Convention Center at 5:30 PM on Monday, October 28 in Room 31 C. Dr. de Jong will be available for media questions and briefing at 8:30 AM Tuesday, October 29 in the on-site press conference room, 27 AB.*

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**Better Cost-Effectiveness and Worker Productivity In Triple DMARD Therapy Versus Methotrexate Monotherapy In Early Rheumatoid Arthritis; Cost-Utility Analysis Of The Treach Trial**

**P.H.P. de Jong**<sup>1</sup>, A.E.A.M. Weel<sup>2</sup>, J.J. Luime<sup>1</sup>, P.J. Barendregt<sup>2</sup>, A.H. Gerards<sup>3</sup>, P.A. van der Lubbe<sup>3</sup>, M.H. de Jager<sup>4</sup>, P.B. de Sonnaville<sup>5</sup>, D. van Zeben<sup>6</sup>, B.A. Grillet<sup>7</sup> and J.M.W. Hazes<sup>1</sup>, <sup>1</sup>Erasmus University Medical Center, Rotterdam, Netherlands, <sup>2</sup>Maastad Hospital, Rotterdam, Netherlands, <sup>3</sup>Vlietland Hospital, Schiedam, Netherlands, <sup>4</sup>Albert Schweitzer Hospital, Dordrecht, Netherlands, <sup>5</sup>Admiraal de Ruyter hospital, Goes, Netherlands, <sup>6</sup>Sint Franciscus Gasthuis, Rotterdam, Netherlands, <sup>7</sup>Zorgsaam Hospital, Terneuzen, Netherlands

**Background/Purpose:** In the treatment in the Rotterdam Early Arthritis Cohort (tREACH) trial we showed that treatment goals were attained faster and maintained with less treatment intensifications within the initial triple DMARD therapy (iTDT) groups as opposed to the initial methotrexate (MTX) mono-therapy (iMM) group. Medication costs are just 20-50% of the total costs. Furthermore the policy for covering prescribed drugs by health insurance companies and governments is more and more influenced by cost-effectiveness. Therefore, our aim is to investigate which initial treatment regimen has the lowest costs per Quality Adjusted Life Year (QALY)

**Methods:** The one-year data of the tREACH trial were used. Patients were included who had a high probability (> 70%) of progressing to persistent arthritis, based on the prediction model of Visser. The Visser algorithm and 2010 criteria for RA have similar discriminative abilities to identify patients at risk of persistent arthritis at 1 year. Patients were randomized into 3 induction therapy strategies: (A) iTDT (MTX 25 mg/week + sulfasalazine 2 grams/day + hydroxychloroquine 400mg/day) with intramusculair glucocorticoids (GCs) (depomedrol 120mg), (B) iTDT with an oral GCs tapering scheme (starting 15 mg) and (C) iMM with oral GCs similar to B. We used a treat-to-target approach, with patients being examined every 3 months and treatment decisions based upon the original DAS thresholds for low disease activity. Data on QALYs, direct and indirect cost were used. Direct costs are the costs of treatment and medical consumption, whereas indirect costs are costs due to loss of productivity (i.e. sick leave and unemployment).

**Results:** A total of 281 patients were randomly assigned to strategy (A) (n=91), (B) (n=93) or (C) (n=97). Average QALYs (ideally 1) for treatment strategy A, B and C are given in table 1. Direct and indirect costs per QALY were higher in the iMM group compared with the iTDT groups (table 1). The difference in direct costs was due to ~40% more biological usage, from 3 months up to 1 year. Less unemployment, long-term sickness and reduction in contract hours caused the difference in indirect costs (table 2). Total costs per QALY differed significantly between treatment arm B and C (p=0.012, table 1).

**Conclusion:** iTDT had the lowest costs per QALY compared with iMM. Furthermore iTDT has significant better worker productivity. This underlines once again why iTDT instead of iMM is preferred as first choice in very early RA.

**Table 1: QALYs and (specified) average cost per QALY after 1 year of follow-up**

	A. MTX + SASP + HCQ + im GCs (n=91)	B. MTX + SASP + HCQ + oral GCs (n=93)	C. MTX + oral GCs (n=97)
QALYs <sup>1</sup> (AUC)	0.75 (0.11)	0.76 (0.10)	0.73 (0.13)
<b>Costs per QALY</b>			
Total direct costs*	€4841 (€7225)	€5099 (€7152)	€7969 (€10307)
• Medication†	€3676 (€6758)	€3872 (€6493)	€6162 (€9618)
• Medical consumption	€1023 (€693)	€1013 (€625)	€1300 (€1264)
• Hospitalization	€143 (€874)	€215 (€1002)	€507 (€3401)
Total indirect costs‡	€7889 (€15339)	€5271 (€11624)	€9388 (€15084)
Total costs§	€12710 (€18737)	€10371 (€15602)	€17357 (€21729)

Results shown are mean(sd).

<sup>1</sup>QALYs are measured with the Dutch EuroQol.

\*p=0.018 and p=0.028 for resp. A. vs C and B vs C. ‡p=0.037 B vs C.

†p=0.043 A vs. C §p=0.012 B vs C.

Abbreviations: AUC, area under the curve; GCs, glucocorticoids; HCQ, hydroxychloroquine; MTX, methotrexate; QALYs, Quality Adjusted Life Years; SASP, sulfasalazine

**Table 2: Loss of productivity and costs during the first year of therapy, stratified for initial treatment regimen.**

	A. MTX + SASP + HCQ + im GCs (n=91)	B. MTX + SASP + HCQ + oral GCs (n=93)	C. MTX + oral GCs (n=97)
Unemployment change*	-1 (-2%)	-4 (-8%)	+6 (+11%)
<b>Loss of productivity</b>			
Sick leave			
o Occurrence	47 (89%)	43 (81%)	46 (81%)
o Long term sickness <sup>1</sup> †	10 (19%)	5 (9%)	17 (30%)
o Days absent, median(IQR)	3 (1 – 8)	5 (1 – 11)	4 (1 – 8)
Reduction contract hours			
o Occurrence	17 (32%)	20 (38%)	22 (39%)
o Decrease in hours, median(IQR)‡	18 (4 – 37)	5 (1 – 11)	29 (10 – 36)

Results shown are number (%) unless stated otherwise.

<sup>1</sup>Long term sickness is defined as absence from work longer than 160 days (Dutch friction period)

\*p=0.015 and p=0.015 for respectively A vs. C and B vs. C.

†p=0.0076 B vs. C.

‡p=0.0007 B vs. C.

Abbreviations: GCs, glucocorticoids; HCQ, hydroxychloroquine; MTX, methotrexate and SASP, sulfasalazine.

**Disclosures: P. H. P. de Jong, None**

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