combination therapy; 3. Initial combination therapy with prednisone; or 4. Initial combination therapy with infliximab. During the 10-year follow-up period treatment was steered at low disease activity (DAS ≤ 2.4) and adjusted every three months when necessary. After 10-years patients were treated and followed-up according to regular care. We explored mortality through the Dutch state registry for mortality (Centrum voor Familiegesciedenis) and treating rheumatologist. Mortality in the BeSt cohort was compared to the general Dutch population (Statistics Netherlands) matched by gender, age and calendar year using the standardized mortality ratio (SMR). Kaplan-Meier curves and the log-rank test were used to compare survival among the initial treatment strategies.

Results: The mean duration of follow-up in non-deceased patients was 17 years (range 16-18). In total, 143 patients died (28%) compared to a total of 105 (21%) expected deaths in the reference population. The overall SMR after 17 years was 1.37 (95% CI: 1.16-1.61). Within the study population, no statistically significant difference in survival-curves was observed between the four initial treatment strategies (log-rank $p=0.76$) (table 1, and figure 1).

Table 1. BeSt study cohort mortality - stratified for initial treatment strategy

	Sequential monotherapy n=126	Step-up combination therapy n=121	Initial combination therapy with prednisone n=133	Initial combination therapy with infliximab n=128
N (%) †	38 (30)	31 (26)	41 (31)	33 (26)
SMR (95% CI)	1.41 (1.03-1.94)	1.20 (0.84-1.70)	1.53 (1.13-2.09)	1.31 (0.93-1.85)

SMR: standardized mortality ratio (number observed deaths/number expected deaths); CI: confidence interval. Conclusion:

Figure 1. Survival curves – stratified for initial treatment strategy

After a mean of 17 years follow-up the mortality was increased in the BeSt study cohort when compared to the general Dutch population. We observed no difference in survival curves among the four treatment strategies.

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OP0220

ASSESSING THE EFFECT OF INCREASED BODY MASS INDEX ON RESPONSE TO TNF INHIBITORS IN ESTABLISHED RHEUMATOID ARTHRITIS: RESULTS FROM THE METEOR DATABASE

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Background: Rheumatoid arthritis (RA) is associated with increased body mass index (BMI)- 60% of patients are either overweight or obese. Obesity in RA has been shown to predict reduced response to biologic therapy including tumour-necrosis-factor inhibitors (TNFi) [1]. However, it is not clear whether increased BMI influences response to all TNFi drugs in RA.

Objectives: 1.To explore whether BMI is associated with response to TNFi in patients with established rheumatoid arthritis (estRA), including those newly-starting on these drugs.

Methods: Participants with estRA (>1year since diagnosis) taking biologic medications, registered on METEOR (international database of RA patients), 2008-2013, were included. EULAR response, DAS28 remission (including components), and treatment regimens were recorded at baseline, 6, and 12 months. WHO definitions of overweight (BMI ≥ 25) and obese (BMI ≥ 30) were explored as predictors of TNFi response (good EULAR response and DAS28 remission) using normal BMI as comparator. Logistic and linear regression models (controlling for age, gender, smoking, and baseline outcomes) and sensitivity analyses were performed. Subgroup analyses were performed for grouped TNFi and individual TNFi (infliximab, IFX; adalimumab, ADA; etanercept, ETN).

Results: 247 patients with estRA were taking a biologic at 6 months, and 231 patients were taking a biologic at 12 months. Obese patients taking any biologic were significantly less likely to achieve DAS28 remission (OR 0.33 [95%CI 0.12-0.80]) or good EULAR response (OR 0.37 [95%CI 0.16-0.81]) after 6 months, compared to those of normal BMI; this was also demonstrated in those co-prescribed methotrexate (DAS28 remission: OR 0.23 [95%CI 0.07-0.62]; good EULAR response: OR 0.39 [95%CI 0.15-0.92]). These associations did not remain statistically significant at the 12 months assessment.

Regarding specific anti-TNF therapies, RA patients treated with monoclonal antibody (-mab) TNFis (IFX/ADA/ GOL) were significantly less likely to achieve good EULAR response at 6 months if they were obese RA (n=38), compared to those of normal weight (n=44) (OR 0.17 [95%CI 0.03-0.59]). A similar non-significant difference was demonstrated for DAS28 remission, and 12-month remission. Specifically, obese individuals were significantly less likely to achieve good EULAR response at 6 months with IFX (OR 0.09 [95%CI 0.00-0.61]; n=20), and significantly less likely to achieve DAS28 remission at 6 months when newly-starting ADA (OR 0.14 [95%CI 0.01-0.96]; n=17), compared to those of normal weight. There were no significant differences in remission outcomes between individuals of different BMI taking ETN. A small number of individuals stopped taking their respective biologic after 6months; reason for cessation was not recorded.

Similar outcomes were seen in patients already established on anti-TNF therapy, with overweight and obese individuals less likely overall to be in DAS28 remission at all time points.

Conclusion: In established RA, obesity is associated with reduced treatment response to -mab TNFi. No association between increased BMI and response to ETA was observed. Using BMI to direct biologic drug choice could prove to be a simple and cost-effective personalised-medicine approach to prescribing.

References:

- [1] Schäfer M, Meißner Y, Kewok J, Berger S, Remstedt S, Manger B, et al. Obesity reduces the real-world effectiveness of cytokine-targeted but not cell-targeted disease-modifying agents in rheumatoid arthritis. *Rheumatology*. 2019 Nov 20.

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OP0221

HAVE 5-YEAR SURVIVAL RATE AND MORTALITY CHANGED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN THE PAST TWENTY YEARS?-RESULTS FROM THE IORRA COHORT

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Background: The mortality of patients with rheumatoid arthritis (RA) had been reported as being worse than that of the general population [1, 2], but is expected to have improved over time because the progress in treatment of RA during the past twenty years has been actively adopted to RA management [3, 4]. However, the change in the mortality still remains controversial in patients with early RA [5, 6].

Objectives: To investigate whether the vital prognosis of patients with early RA has changed in the past twenty years.

Methods: The IORRA cohort is a large observational cohort established in 2000 at the Institute of Rheumatology, Tokyo Women's Medical University. Essentially, all Japanese patients diagnosed with RA at our institute were registered and clinical parameters were assessed biannually. As there is no National Death Registry in Japan, we obtained death report from residual families who responded to our mail query to patients who failed to conduct the subsequent IORRA survey, from physicians of affiliated hospitals and from police in case they found dead

patient outside of a hospital. In this study, the patients with early RA (less than 2 years of disease duration) who participated in the survey for the first time from 2001 to 2012 were included and observed for five years from the date of the initial survey. We classified patients into group A (enrolled in 2001-2006) and B (enrolled in 2007-2012). Five-year survival rate and standardized mortality ratio (SMR) were calculated for each group. SMR was calculated using the life tables in Japanese general population reported by the Ministry of Health, Labour and Welfare, Japan. The effects of loss to follow-up cases were evaluated by multiple imputation method as a sensitivity analysis of SMR.

Results: A total of 3,217 patients with early RA were analyzed. The number of patients was 1,609 (79.4% female) in the group A and 1,608 (81.8% female) in B. The median age at baseline was 55 in both groups. Among a total of 3,217 patients, 486 (15.1%) patients were lost during 5-year follow-up; 213 (13.2%) in the group A and 273 (17.0%) in B, respectively. During the observational period, deaths were confirmed in 47 cases (2.9%) in the group A and 45 (2.8%) in B. Major causes of death included malignancies (28% in the group A, 38% in B), respiratory involvement (23% in the group A, 40% in B), cerebrovascular disorders (11% in the group A, 2% in B), and cardiovascular disorders (11% in the group A, 0% in B). The five-year survival rate was 88.8% for the group A and 87.8% for B, and the SMR was 0.81 (95%CI: 0.59-1.08) for the group A and 0.78 (0.57-1.04) for B when assuming all the lost to follow-up patients were alive for 5 years. In the sensitivity analysis assuming that the mortality rate of patients who were lost to follow-up was twice as that of the general population, the SMR was 0.90 (0.68-1.19) for the group A and 0.92 (0.68-1.23) for B.

Conclusion: The mortality of patients with early RA in the past twenty years has been comparable to that of the Japanese general population. In addition, the SMR and the five-year survival rate did not change overtime.

References:

- [1] Cobb, S., et al. *N Engl J Med* 1953; 249(14): 553-556.
- [2] Nakajima, A., et al. *Scand J Rheumatol* 2010; 39(5): 360-367.
- [3] Smolen, J. S., et al. *Ann Rheum Dis* 2014; 73(3): 492-509.
- [4] Singh, J. A., et al. *Arthritis Care Res* 2016; 68(1): 1-25.
- [5] Lacaille, D., et al. *Ann Rheum Dis* 2017; 76(6): 1057-1063.
- [6] Humphreys, J. H., et al. *Arthritis Care Res* 2014; 66(9): 1296-1301.

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OP0222

IS REFERRING EARLY ARTHRITIS PATIENTS WITHIN 6 WEEKS ASSOCIATED WITH BETTER LONG-TERM OUTCOMES THAN REFERRING WITHIN 12 WEEKS AFTER SYMPTOM ONSET? – INVESTIGATING THE EVIDENCE FOR THE FIRST EULAR RECOMMENDATION FOR EARLY ARTHRITIS IN TWO OBSERVATIONAL COHORTS

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Background: EULAR- recommendations for management of early arthritis formulated that patients should be referred to, and seen by a rheumatologist, within 6-weeks after symptom onset. The mentioned period of ≤6-weeks after symptom onset is shorter than ≤12-weeks, the period that is generally considered as the 'window-of-opportunity'. Because implementation provides challenges, and evidence supporting that referral ≤6-weeks is better than e.g. <12-weeks is missing, we investigated if ≤6-weeks relates to improved long-term outcomes.

Objectives: We used an observational study design to investigate in two cohorts if time-to-encounter (TtE) a rheumatologist ≤6-weeks, compared to 7-12-weeks, results in better disease long-term outcomes, measured with sustained DMARD-free remission (SDFR) and radiographic progression.

Methods: Consecutive 1987-RA patients of the Leiden EAC (n=1025) and ESPOIR (n=514) were studied during median 7 and 10 years follow-up. Patients were categorized on duration between symptom onset and first encounter with a rheumatologist; ≤6-, 7-12-, and >12-weeks. Multivariable Cox regression (SDFR), linear mixed models (radiographic progression), and meta-analyses were used.

Results: Leiden RA-patients encountered the rheumatologist within 6-weeks obtained SDFR more often than patients seen within 7-12-weeks (HR 1.59, 95%CI:1.02-2.49), and >12-weeks (HR 1.54, 95%CI:1.04-2.29). In ESPOIR, similar but non-significant effects were observed; meta-analysis showed that within 6-weeks was better than 7-12-weeks (HR 1.69, 95%CI:1.10-2.57, Figure 1-A) and >12-weeks (HR 1.67, 95%CI:1.08-2.58). Patients encountered the rheumatologist within 6-weeks had similar radiographic progression than those seen 7-12-weeks, in any cohort, or meta-analysis (Figure 1-B).

Figure 1 Meta-analyses of time-to-encounter the rheumatologist and the chance of achieving sustained DMARD-free remission (A) and radiographic progression (B)

Conclusion: Scientific evidence underlying the first EULAR recommendation depends on the outcome of interest; visiting a rheumatologist within 6-weeks of symptom-onset had clear benefits for achieving SDFR, but not for radiographic progression.

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