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OP0263 INFLAMMATORY RHEUMATIC DISEASES HAVE BROAD IMPACT ON REPRODUCTIVE HEALTH – A NATIONWIDE EVALUATION AND SYSTEMATIC COMPARISON ACROSS RHEUMATIC DISEASES

Keywords: Pregnancy and reproduction

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Background: Inflammatory rheumatic diseases (IRDs) affect men and women of reproductive age. The lack of reproductive health studies on IRDs hinders making evidence-based recommendations on fertility preservation, prevention of pregnancy complications, and management of the IRDs during reproductive years.
Objectives: To systematically estimate the impact of IRDs on diverse reproductive outcomes and compare the effects to those observed for other immune-mediated inflammatory diseases.
Methods: The total Finnish population (FinRegistry; N=5,339,804) was linked to nationwide registries (inpatient and outpatient care, and Medical Birth Register covering all live births since 1987, N=1,920,411 births). We focused on seropositive and seronegative rheumatoid arthritis (RA), ankylosing spondylitis (AS), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), and Sjögren syndrome (SS), selecting individuals born 1964–1984 diagnosed with the IRD before age 30, and 20 sex, birth-year, and education level-matched controls. The patterns were compared to a range of other immune-mediated inflammatory diseases, such as type 1 diabetes, inflammatory bowel disease, and hypothyroidism.
Results: The case count of women with an IRD ranged from 412 for PsA to 1,487 for seropositive RA (mean age range at diagnosis 11.0 in JIA to 25.7 in AS). Women with IRD experienced a higher prevalence of childlessness than controls (mean difference 4.2%, largest in JIA at 9.3%), had fewer children (mean 0.2 fewer, highest in JIA at 0.3 fewer), and the start and end of reproduction were slightly shifted towards an earlier age. Also men with an IRD experienced a higher prevalence of childlessness than controls (mean difference 4.1%, largest in SLE at 11.0%). Overall, the impact was similar in other immune-mediated inflammatory diseases in both women and men, with high variability between diseases. For maternal health conditions, five IRDs showed an elevated risk for pre-eclampsia, with the largest effect size observed for SLE (OR 2.65, 95%CI 1.94–3.62). No elevated risk was observed for gestational diabetes in any of the IRDs. Many of the IRDs were associated with at least one of the ten evaluated adverse perinatal outcomes, such risk of nonelective Caesarean section, and admission to neonatal ICU (**Figure 1**), with the largest effect sizes observed for SLE and SS.

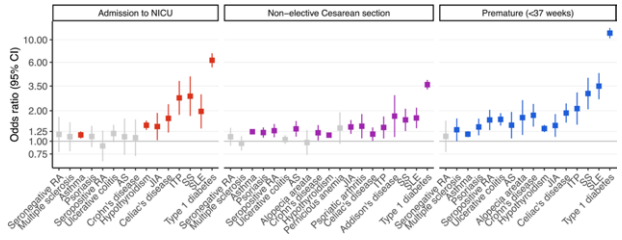

Figure 1. Systematical analysis of perinatal outcomes, with results shown for three of the ten evaluated perinatal outcomes. Results are shown for diseases with over 20 cases for the outcome and associations with p-value >0.05 are shown in gray. NICU = neonatal ICU, ITP = immune thrombocytopenic purpura.

Conclusion: In this comprehensive, nationwide evaluation of reproductive health metrics, we observed widespread impact of IRDs on reproductive health. The effects were comparable to many other immune-mediated inflammatory diseases, but we also observed high variability between diseases. Overall, these findings emphasize the need for further research, and the importance of counseling on reproductive health in both men and women with IRDs.
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OP0264 COST-UTILITY OF A PROGRESSIVE SPACING OF TOCILIZUMAB OR ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED REMISSION: A MEDICO-ECONOMIC ANALYSIS OF THE TOLEDO TRIAL

Keywords: Clinical trials, bDMARD, Rheumatoid arthritis

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Background: Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) progressive tapering is a real opportunity in people living with rheumatoid arthritis (RA) having achieved remission both from the patient and the Society perspectives. The ToLEDo (Towards the Lowest Efficacious Dose) trial aimed to assess a disease activity-driven progressive tapering strategy of tocilizumab (TCZ) or abatacept (ABA) compared to their maintenance at full dose in RA patients in sustained remission. Non-inferiority (NI) was not demonstrated in terms of disease activity (primary endpoint) nor relapses, major relapses, radiographic progression (secondary endpoints) [1].
Objectives: The aim of this secondary analysis was to assess the cost-utility of the spacing strategy (S-arm) in the ToLEDo trial compared to full dose maintenance (M-arm).
Methods: The ToLEDo trial is a multicenter 2-year NI randomized open-label controlled trial, which enrolled 228 patients (113 in the S-arm and 115 in the M-arm). A cost-utility analysis was conducted on the per protocol population. In each arm, health benefits were estimated every 6 months by Short Form Health Survey (SF-6D) and EuroQoL (EQ-5D)-derived utility measurements. Cost elicitation integrated health resource use including bDMARD costs (direct cost) as well as productivity loss (indirect cost) using the friction cost method. The incremental cost-utility ratios (ICUR) were calculated by dividing the difference of costs between S-arm and M-arm by the difference of utilities between the 2 arms. 95% confidence interval (95%CI) were calculated by bootstrap (20,000 iterations). The incremental net benefit (INB) was calculated for willingness to pay (WTP) values ranging from 0 to 150,000€. The analyses were replicated using SF-6D (primary analysis) or EQ-5D, and in ABA and TCZ subgroups. Acceptability analyses as well as stochastic sensitivity analyses (simulating costs and utilities using MCMC algorithms) were also performed.
Results: Overall, 178 patients were included (82 in S-arm, 96 in M-arm) in the per protocol analysis. At the end of the follow-up in the S-arm, 15.0% of patients discontinued their biologic, 48.7% spaced the injections, and 36.3% remained at the standard dose. The difference in terms of two-years utility gains between S-arm and M-arm was 0.004 (95%CI -0.012, 0.021) with SF-6D. The difference of total costs between S-arm and M-arm was -4,275 € (95%CI -5,955 to -2,542). The estimated ICUR of the spacing strategy over the maintenance at full dose was €932,003 saved per QALY (95% CI -7,534,788 to 6,720,372) with SF-6D. The INB was 4,734.6€ for a WTP of 100,000€. With a willingness to accept of 0 €/QALY lost, the probability to be cost-effective for the spacing strategy was 70.6% (***Figure 1***). The results were consistent when using EQ-5D-derived utilities, in ABA and TCZ subgroups, as well as in the stochastic sensitivity analyses (***Table 1***).
Conclusion: Although the ToLEDo trial did not demonstrate non-inferiority, the tested disease activity-driven tapering strategy was not associated with health loss in terms of utilities and incurred for substantial cost savings, making this strategy potentially dominant.
REFERENCE:
[1] Kedra J, Dieudé P, Marotte H et al. Towards the Lowest Efficacious Dose (ToLEDo): Results of a Multicenter Non-Inferiority Randomized Open-Label Controlled Trial Assessing Tocilizumab or Abatacept Injection Spacing in Rheumatoid Arthritis Patients in Remission [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10).

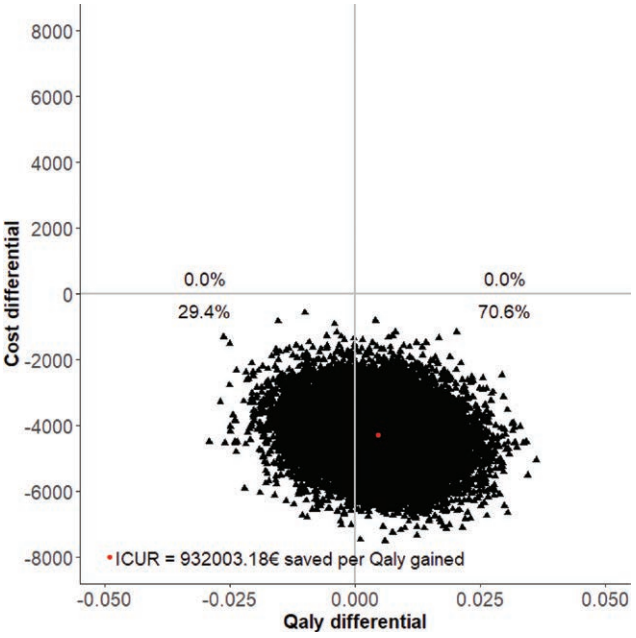

Figure 1. cost-utility plane (spacing versus maintenance), with utilities derived from PP SF-6D

Table 1. ICUR in ABA subgroup, TCZ subgroup, using EQ-5D-derived utilities, and stochastic sensitivity analysis

	ABA subgroup (PP SF-6D)	TCZ subgroup (PP SF-6D)	PP EQ-5D	Stochastic sensitivity analysis (PP SF-6D)
ICUR, €/QALY gained	-420,076.22 (95%CI -1,044,462 ; 1,461,037)	-1,008,225 (95%CI -2,436,237; 1,898,967)	-52,005 (95%CI -458,934; 369,967)	-481,029.28 (95%CI -1,300,747; 1,867,263)

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OP0265

WORK PARTICIPATION AND THE COVID19 PANDEMIC: A DUTCH PROSPECTIVE COHORT STUDY IN PEOPLE WITH INFLAMMATORY RHEUMATIC DISEASES AND HEALTHY CONTROLS

Keywords: COVID, Work-related issues

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Background: People with inflammatory rheumatic diseases (iRD), such as rheumatoid arthritis (RA) and spondyloarthritis (SpA), experience restrictions in work participation. In times of crisis, such as the coronavirus disease 2019 (COVID19) pandemic, people with iRD might be more vulnerable for adverse work outcomes (i.e. (partial) job loss and sick leave) and restrictions in work ability while at work.

Objectives: To (a) compare occurrence of adverse work outcome (AWO) and change in work ability during the first two years of the pandemic (2020-2022), as well as current (2022) work ability, between people with iRD and healthy controls in the Netherlands; (b) understand which subgroups of patients are most vulnerable to incur work participation outcomes; and (c) explore the role of remote work characteristics on work performance.

Methods: Data from a Dutch longitudinal study on COVID19 at Reade and Amsterdam UMC were used. Information about work was collected at one fixed timepoint. Patients (18-67 years) with iRD and controls were asked in March 2022 to answer questions on work participation and their work situation in March 2020 (pre-pandemic; retrospectively) and March 2022 (current). AWO was defined as any of: (1) shift between 2020-2022 from employment to unemployment; or from full to part-time employment; (2) reduction in working hours; (3) ongoing long-term sick leave. Work ability (change and current) was assessed with the Work Ability Index (range 0 [worst] to 10 [best]). Outcomes were compared between groups (iRD vs control) with statistical tests. Multivariable logistic or linear regression analyses were used to explore the associations between iRD and AWO or (change in) work ability. Interactions (effect modification) were tested and, if present, analyses were stratified. The role of remote work factors on remote work performance was described.

Results: In total, 1,438 iRD patients and 526 controls of working age (18-67) participated. The majority was female (67%) and was employed pre-pandemic (69% patients, 84% controls). Patients mainly had RA or SpA (85%). In pre-pandemic employed subjects, 227 patients (23%) and 79 controls (18%) experienced AWO (p=0.04). Only 35 patients (4%) and 12 controls (2%) of these, attributed this to COVID (impact by personal health or national pandemic measures; p=0.36). Logistic regressions of AWO were stratified because of interactions between group and sex, comorbidities or a physically demanding job. In all models, patients were more likely than controls to experience AWO (range OR 1.63 to 3.34 across models, Figure 1), and especially patients with comorbidities or a physically demanding job. Of note, COVID-related AWO was not significantly more likely in patients (OR=1.62, 95%CI 0.80-3.27). Change in work ability during the pandemic did not differ between groups (-0.3 (SD 1.8) patients vs -0.2 (SD 1.6) controls, p=0.38), and regression analyses also did not reveal significant differences. Linear regression of current work ability (stratified by sex due to interaction) showed female patients compared to female controls experienced lower work ability (B=-0.66; 95%CI -0.92 to -0.40), while this was not observed in males. Past SARS-CoV-2 infection was not associated with AWO/work ability. When working remotely, care for children and absence of colleagues had both positive (19% and 24%, resp.) and negative (34% and 57%, resp.) influence on work performance, while employer support and reduced commuting time had positive influence (83% and 86%, resp.).

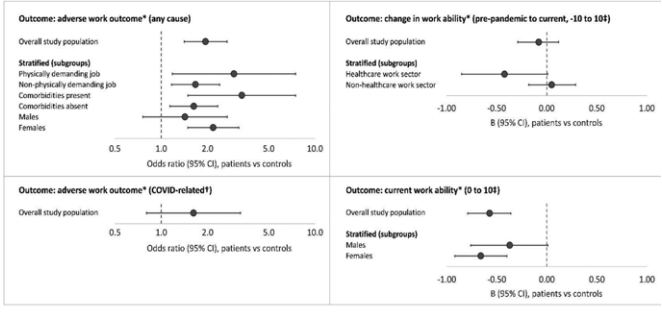

Figure. Association between group (patients vs controls) and adverse work outcome or (change in) work ability. An odds ratio >1 or a B <0 indicate a worse outcome in patients compared to controls (occurrence of adverse work outcome, a greater decrease in work ability or lower current work ability). *Covariables explored in models (forward method, retained if confounder for group and outcome, or if significantly associated with outcome): age, gender, education, comorbidities, past COVID infection, COVID vaccination, work sector, job demands, employment contract, working hours per week, work location. †COVID-related adverse work outcome defined as adverse work outcome attributed by the patient to either impact of COVID on personal health or impact of national pandemic measures.

Conclusion: During the COVID pandemic, patients experienced more AWO than healthy controls, and especially patients with physically demanding jobs and comorbidities were at higher risk. However, the frequency of COVID-related AWO was low and did not differ substantially between patients and controls. A likely explanation is that the governmental support for employers protected those in vulnerable positions, such as patients with iRD.

REFERENCES: NIL.

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