Sex Differences in Autoimmune Multimorbidity Across 11 Autoimmune Disorders in the Real-World Setting in Germany

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Background and Objective

- While most studies have focused on the incidence, pathogenesis, and severity of individual autoimmune diseases (AIDs), less attention has been paid to *autoimmune multimorbidity* — the co-occurrence of multiple AIDs within the same individual.
- The present study aims to analyse sex differences in autoimmune multimorbidity across eleven AIDs in a real-world setting.

Methods

This study utilized electronic medical records from the IQVIA Disease Analyzer database, which includes electronic medical records of outpatients recorded in private practices. The data include baseline demographic variables, such as age and sex, diagnoses, and prescriptions [1].

This retrospective cross-sectional study included **164,596 individuals** who visited one of **1,037 primary care physicians** in **2024** (see **Figure 1**).

All patients had been diagnosed with at least one of **eleven predefined AIDs** between 2020 and 2024. For each AID, the proportions of **autoimmune multimorbidity** were descriptively compared between **female and male** patients.

To compare the proportions of autoimmune multimorbidity between women and men **chi-squared tests** were conducted, and **a two-sided p-value of <0.05** was considered statistically significant. Other analyses were performed descriptively without hypothesis testing.

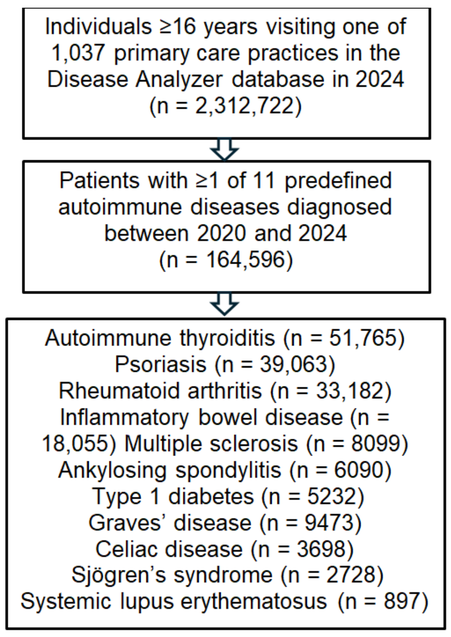

Figure 1: Flow diagram of patient selection and inclusion across eleven autoimmune diseases (AIDs).

Results

- The total number of patients varied widely across conditions.
- The highest counts were observed **for autoimmune thyroiditis** (n = 51,765), **psoriasis** (n = 39,063) **and rheumatoid arthritis** (n = 33,182), while the lowest were for systemic lupus erythematosus (n = 897) and Sjögren's syndrome (n = 2,728) (see **Table 1**).
- A notable **sex disparity** was present in several conditions. For example, 30.2% of women but only 25.4% of men with **systemic lupus erythematosus**, 31.6% of women and 20.7% of men with **Sjögren's syndrome**, 28.5% of women and 18.6% of men with **ankylosing spondylitis**, and 20.7% of women versus 12.5% of men with celiac disease had at least **one additional AID** (see **Figure 2**).
- Conversely, **autoimmune thyroiditis** and **rheumatoid arthritis exhibited smaller sex-related differences** in autoimmune multimorbidity (see **Figure 2**).

Table 1: Basic characteristics of the study patients.

Disease	Number of patients	Age (mean, SD)	Female (N,%)	Male (N, %)
Psoriasis	39,063	59.2 (16.9)	20,194 (51.7)	18,869 (48.3)
Rheumatoid arthritis	33,182	65.3 (15.4)	22,649 (68.3)	10,533 (31.7)
Systemic lupus erythematosus	897	54.1 (16.6)	771 (86.0)	126 (14.0)
Autoimmune thyroiditis	51,765	54.1 (16.5)	44,039 (85.1)	7,726 (14.9)
Inflammatory bowel disease	18,055	53.2 (18.0)	9,757 (54.0)	8,298 (46.0)
Multiple sclerosis	8,099	52.7 (15.7)	5,653 (69.8)	2,446 (30.2)
Celiac disease	3,698	46.5 (18.2)	2,689 (72.7)	1,009 (27.3)
Ankylosing spondylitis	6,090	57.2 (16.1)	2,706 (44.4)	3,384 (55.6)
Type 1 diabetes	5,232	58.9 (19.3)	2,142 (40.9)	3,090 (59.1)
Graves' disease	9,473	57.7 (16.8)	7,550 (79.7)	1,923 (20.3)
Sjögren's syndrome	2,728	64.8 (16.2)	2,106 (77.2)	622 (22.8)

Results

Autoimmune multimorbidity by disease and sex

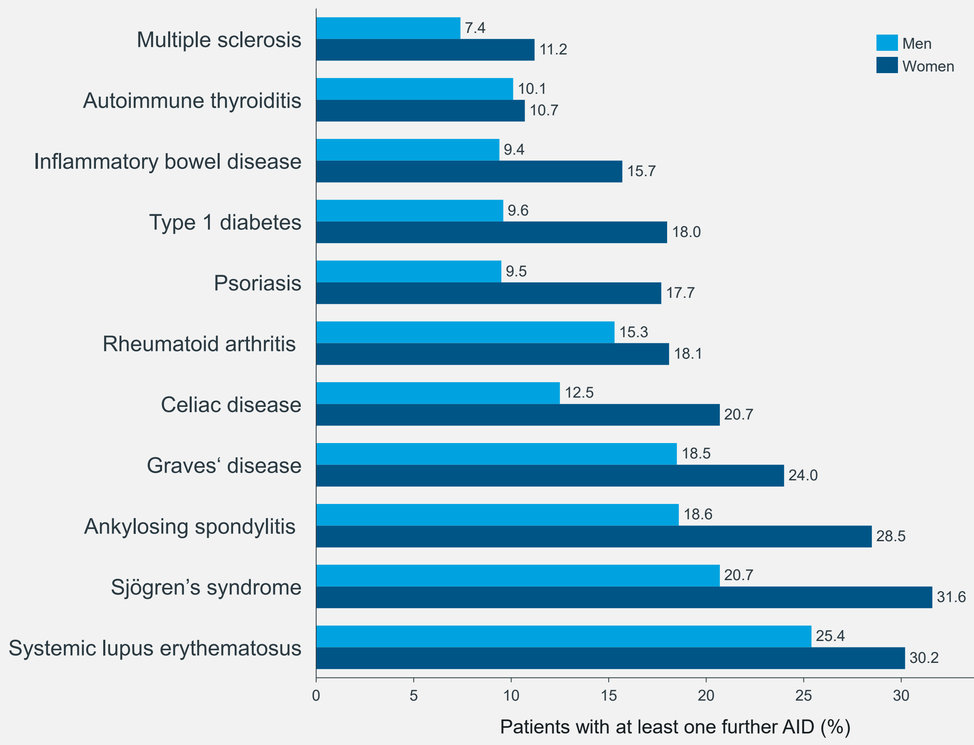

Figure 2: Proportion of patients with at least one additional autoimmune condition by primary condition and sex.

Most frequent coexisting autoimmune disorders

Table 2: Most frequent coexisting autoimmune disorder among patients with predefined auto-immune disorders.

Disease affected by polyautoimmunity	Most frequent coexisting AID	Proportion of patients with a co-diagnosis (%)	
		Women	Men
Psoriasis	Rheumatoid arthritis	7.9	4.7
Rheumatoid arthritis	Psoriasis	7.1	8.4
Systemic lupus erythematosus	Rheumatoid arthritis	17.5	10.3
Autoimmune thyroiditis	Rheumatoid arthritis	3.1	1.9
Inflammatory bowel disease	Rheumatoid arthritis	5.0	2.8
Multiple sclerosis	Autoimmune thyroiditis	4.5	0.9
Celiac disease	Autoimmune thyroiditis	11.0	2.9
Ankylosing spondylitis	Rheumatoid arthritis	14.5	8.7
Type 1 diabetes	Autoimmune thyroiditis	7.7	2.2
Graves' disease	Autoimmune thyroiditis	15.7	10.3
Sjögren's syndrome	Rheumatoid arthritis	14.0	8.8

Odds ratio of autoimmune multimorbidity (females vs. males)

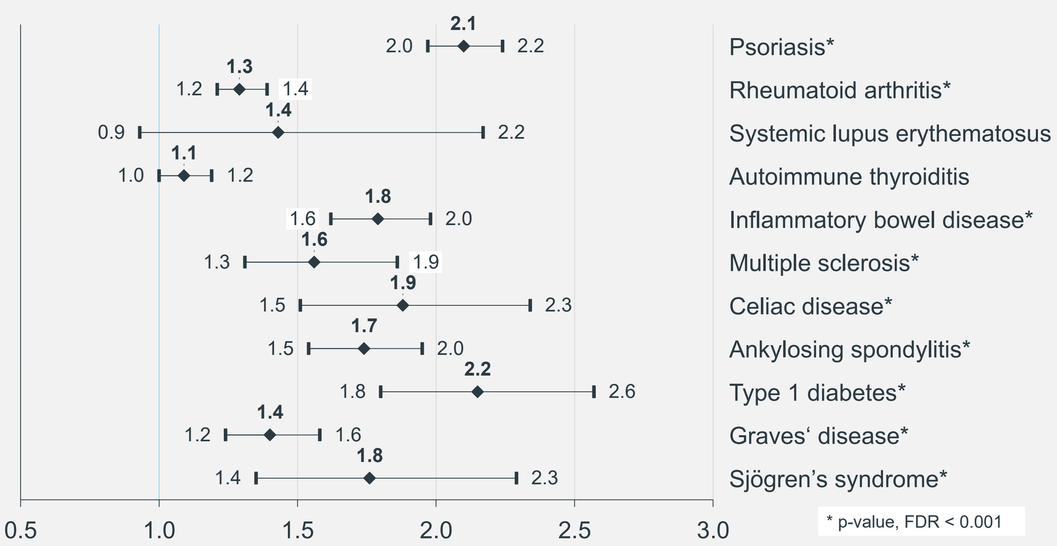

Figure 3: Multivariable logistic regression of autoimmune multimorbidity (≥ 1 other autoimmune disease) by index autoimmune disease, adjusted for age and clustering by practice. OR with 95 % CI.

Conclusion

Clinical Implications: This study highlights significant sex differences in autoimmune multimorbidity among individuals with predefined AIDs in a real-world primary care setting. These findings support the hypothesis that women may have a heightened susceptibility to co-occurring autoimmune conditions, potentially due to underlying hormonal, genetic, or immunological factors.

Study Limitations: Limitations include the cross-sectional study design, potential misclassification due to ICD-10 coding, and lack of information on disease course, lifestyle, and family history. Furthermore, results are primarily generalizable to German outpatient care.

Future Directions: These results underscore the clinical relevance of routinely monitoring for multiple autoimmune diagnoses, particularly among female patients, to support earlier detection and more personalized care strategies. Future research should use longitudinal data to further investigate temporal patterns and mechanisms of multimorbid development in autoimmune diseases, with particular attention to sex-specific differences.

References: [1] Rathmann W, Bongaerts B, Carius HJ, Kruppert S, Kostev K. Basic characteristics and representativeness of the German Disease Analyzer database. Int J Clin Pharmacol Ther. 2018 Oct;56(10):459-466. doi: 10.5414/CP203320

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