# High burden of disease for AAV patients in Germany - a claims data study

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## Background and Objectives

**AAV is a rare systemic disease, characterized by recurrent episodes of inflammation. Current therapeutic options are based on high dose glucocorticoids, immunosuppressants, and cytostatic drugs, which impose an additional risk for patients due to high short- and long term toxicity.**

**The aim of this study is to better understand the burden of disease for patients affected by AAV in Germany. Therefore, selected aspects, such as e.g. relapse rates, steroid dosages, hospitalization and mortality rates, were systematically assessed in a claims data study.**

## METHODS

**GERMAN SHI.** In Germany, health insurance is mandatory. Approx. 87 % of the German population is insured via SHI. Vifor worked with Elsevier who cooperate with over 63 SHI companies distributed all over Germany. They cover approximately 7 million insured persons (10% of total insured population). For each patient, all data are longitudinally linked over a period of 6 years (2011-2016). From this pool, data from an age- and gender stratified representative cohort of approx. 4 million German insured persons were analyzed.

**InGef database.** The InGef database holds relevant information from German SHI companies. Key information includes patient level data including demographics, ambulatory/stationary care detail, medication, medical aids and incapacity to work.

**Study parameters.** Patients with Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) were identified through ICD-10 coding. Patient relevant data from 2011-2016 were accessed, and patients with a GPA/MPA diagnosis in 2013 were identified and followed up for the next 3 years. All patients analyzed were continually observable over this time period. Patient records must have been observable between 2011-2016 or deceased and patients must be 18 years or older at time of diagnosis.

### Data parameters accessed within the InGef database.

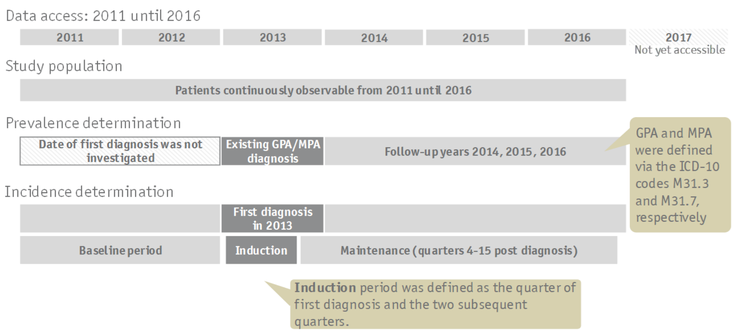


**Figure 1.** Data between 2011-16 was accessed from the InGef database. All patients analyzed were continually observable over this time period. Prevalence and incidence were determined and patient level data analyzed in the aggregate.

InGef: Institute for Applied Health Research

## RESULTS

### The frequency of GPA and MPA increases with age.

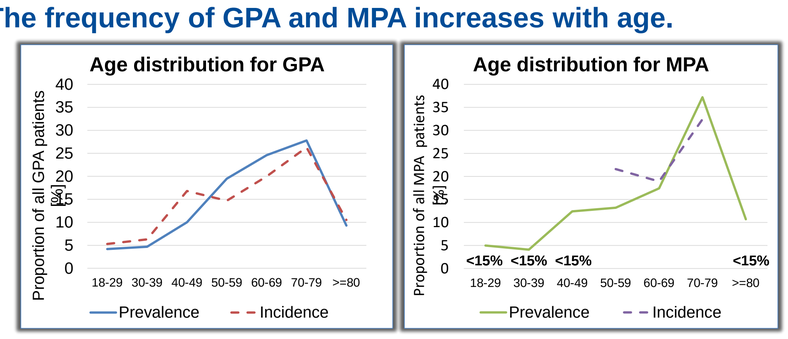


**Figure 2.** As observed in previous publications (1), the frequency of ANCA-associated vasculitis (GPA and MPA) increased with age and reached a peak in the 8th decade in the observed German patient cohort.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis

### Relapses occur in 5 to 8 % of patients every year.

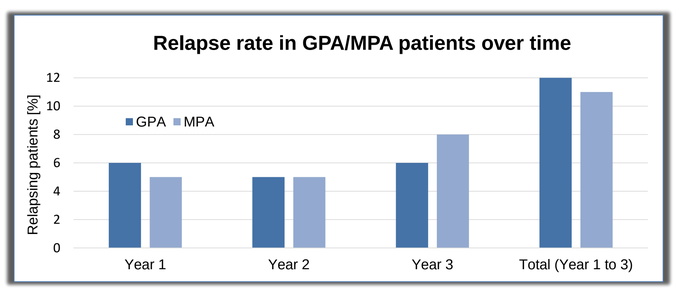


**Figure 3.** 11-12 % of GPA and MPA patients had a relapse within 4 years after diagnosis. No difference in relapse frequency was observed between GPA and MPA in this observation period. Relapses were defined as new temporary prescription of high dose corticosteroids (ambulant) combined with RTX or CYC and/or temporary increased dosing of preexisting corticosteroids (ambulant) combined with RTX or CYC. The time refers to years post GPA/MPA diagnosis.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis, CYC: Cyclophosphamide, RTX: Rituximab

## RESULTS

### Severe kidney damage is a frequent issue in patients with GPA and MPA, especially early after diagnosis.

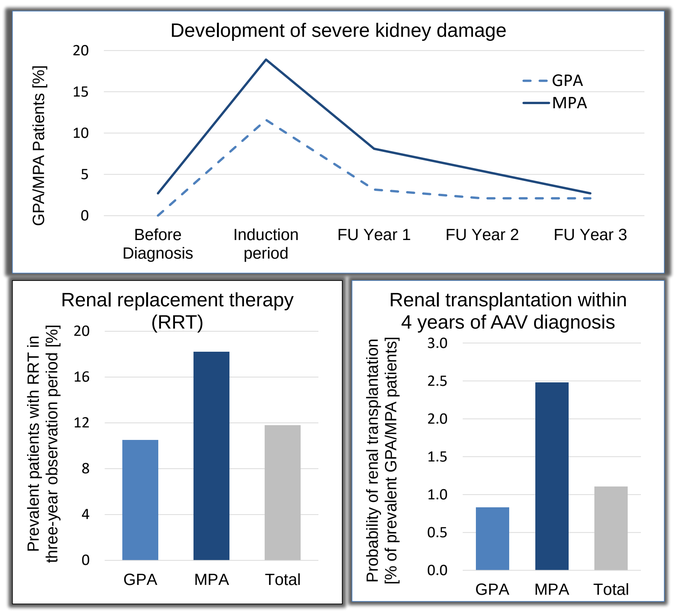


**Figure 4.** AAV diagnosis is associated with a risk to develop severe kidney damage, defined as chronic kidney disease stage III, IV and V (ICD N18.3/.4/.5) as well as renal replacement therapy. This risk is especially pronounced in the first three quarters post diagnosis ("induction period") and decreases over the next 3 years. Renal replacement therapy was necessary in 10 % (GPA) and 18 % (MPA) of patients. Within the observation period of 4 years post diagnosis, 0.8 % of GPA patients and 2,5 % of MPA patients received a renal transplant.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis. AAV: ANCA associated vasculitis. RRT: renal replacement therapy

### Steroid consumption in patients with GPA/MPA is high and decreases over time.

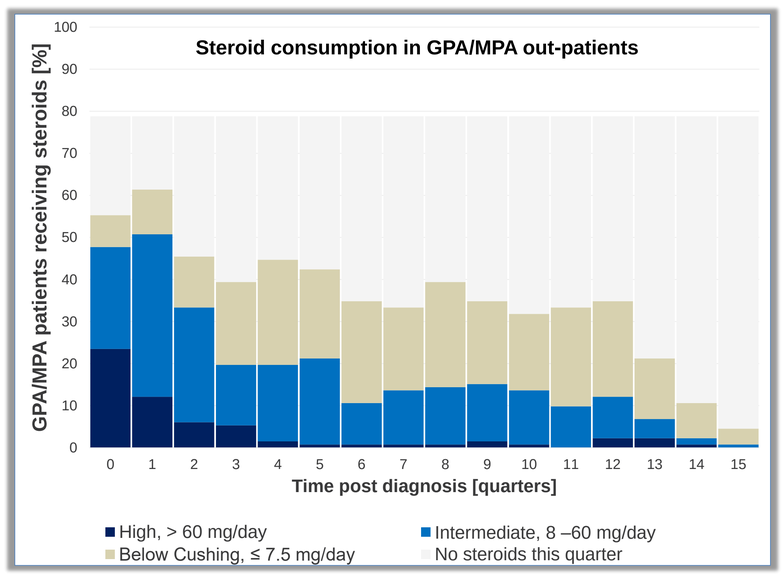


**Figure 5.** Approximately 48 % of newly diagnosed AAV patients received medium (defined as 8-60 mg/day) or high dosed steroids (defined as >60 mg/day) from ambulant care upon diagnosis. In the first three years post diagnosis, the rate of high dose steroids decreased towards zero. However, up to 20 % of the patients were still treated with steroids above the Cushing threshold of 7.5 mg/day. At the same time, roughly 25 % of the patients were treated with low dose steroids (<7.5 mg/day) in this time frame. 79% of all patients received steroids in ambulant care in a 4 year period post diagnosis (light grey).

Note: Due to technical limitations, the current analysis does not include inpatient steroid consumption, so the true burden of usage and cumulative dosage are potentially significantly higher.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis

### Approximately one third of all GPA/MPA patients developed a serious infection requiring inpatient therapy or were infected while being treated in the hospital.

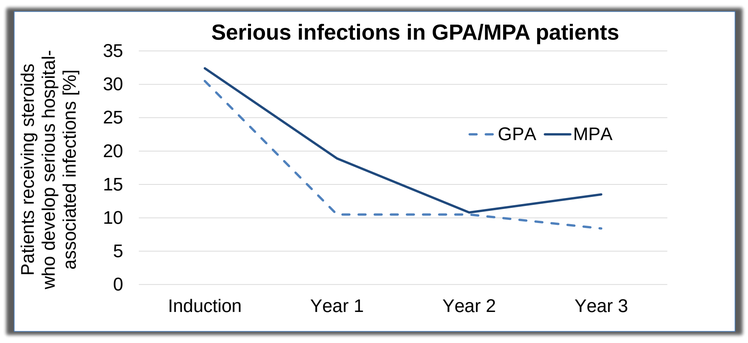


**Figure 6.** In the induction period of AAV therapy (first 3 quarters post diagnosis) approx. 1/3 of all patients developed a serious hospital-associated infection. In the following years the incidence of severe infections decreased to approx. 10%. Severe infections are a risk for both GPA and MPA. Patients have a 42% and 50% risk of developing an infections within a 4 year period, respectively.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis, AAV: ANCA-associated vasculitis

## RESULTS

### The most common co-morbidities in GPA patients are more frequent than in the general SHI population.

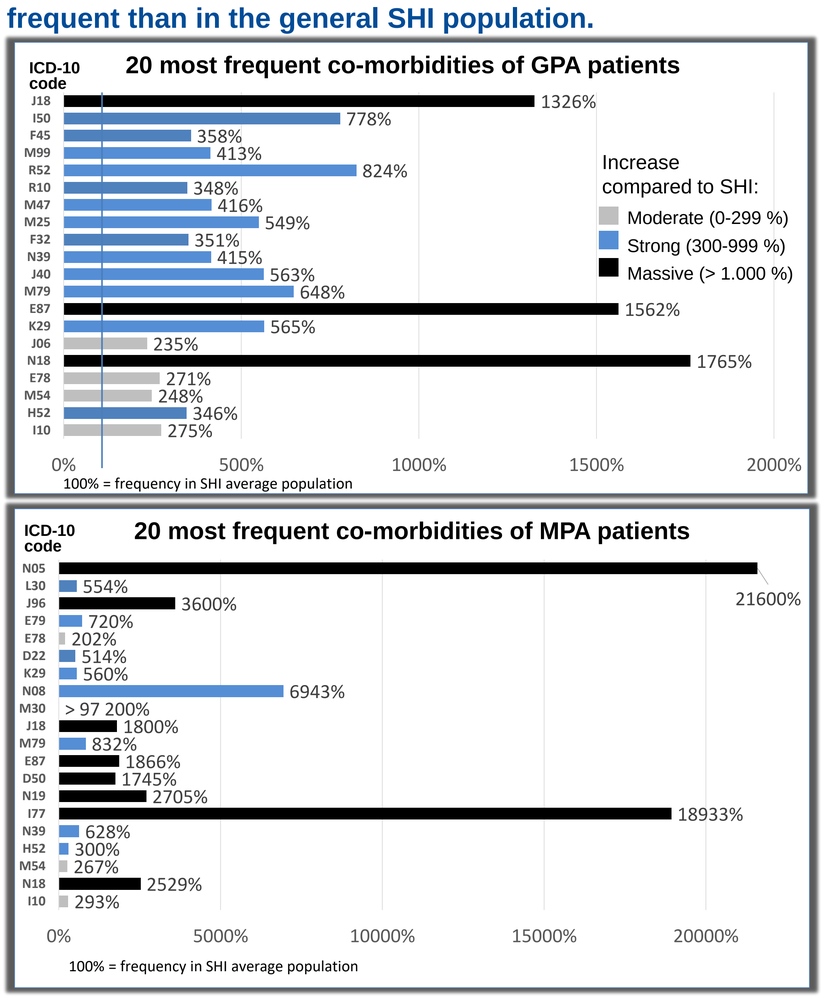


**Figure 6.** All identified top 20 co-morbidities are found more frequently in GPA/MPA patients, than in the general SHI population.

GPA patients show a strong increase in glomerular disorders (N18), pneumonia (J18), and disorders of lipoprotein metabolism and other lipidemias (E78).

MPA patients show a dramatic increase in renal disorders nephritic syndrome (N05) and glomerular disorders (N08), „other" disorders of arteries and arterioles (I77), and respiratory failure (J96). Other disorders of the endocrine (E), respiratory (J), and renal (N) system, are also massively increased in MPA patients.

Roughly half of the 20 co-morbidities of GPA and MPA overlap. Those include among others hypertension (I10), heart failure (I50), disorders of fluid, electrolyte and acid-base balance (E87) and disorders of the urinary system (N39).

SHI = German statutory health insurance.

### Renal impairment poses a strong mortality risk for AAV patients.

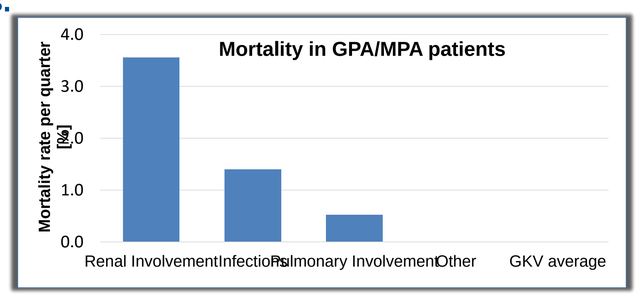


**Figure 7.** Each quarter, 3.6 % of AAV patients who develop a severe kidney disease during hospitalization succumb to disease each quarter. Thus, renal involvement is the strongest risk factor for AAV (GPA+MPA) patients. Patients with severe infections (ICD Chapters A and B+R65) and pulmonary involvement (defined by ICD-10 coding as J00-J22 or J40-J99) showed a 1,4 / 0,5 % chance of mortality per quarter, respectively.

GPA: Granulomatosis with Polyangiitis, MPA: Microscopic Polyangiitis. AAV: ANCA associated vasculitis. ICD-10: International Statistical Classification of Diseases and Related Health Problems, version 10

## CONCLUSIONS

**Patients affected by AAV (GPA or MPA) struggle with a high burden of disease and the risk of serious complications, such as renal failure and strongly increased mortality. In addition, contemporary therapy, based on strong systemic immunosuppressants (steroids) and cytostatics, causes long-term complications. Even with current therapeutic options, relapse and mortality rates are still alarmingly high. The presented study indicates, that the burden of AAV is likely underestimated und might be more severe than previously thought. Hence, new therapeutic approaches are desperately needed.**

**REFERENCES.** **(1) Reinhold-Keller E, Herlyn K, Wagner-Bastmeyer R, Gross WL. Stable incidence of primary systemic vasculitides over five years: results from the German vasculitis register. Arthritis Rheum. 2005;53(1):93-9.**

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