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Characterizing the burden and unmet need of membranous nephropathy

Francesca Barion[a], Glenn Phillips[b], Vasileios Pardalidis[c], James Beggs[c], Ally Robert[c], Smarth Lakhanpal[c], Catherine Kielar[c]

[a]argenx srl, Milan, Italy; [b]argenx BVBA, Gent, Belgium; [c]Avalere Health, Knutsford, UK

Introduction and objectives

- Membranous nephropathy (MN) is a type of glomerular disease that causes nephrotic syndrome, leading to progressive renal impairment. MN can have various underlying causes, including autoimmune disorders, infections, use of certain medications, and exposure to certain toxins; is classified into primary (75%-80%, pMN) and secondary (20%-25%, sMN); and is the second most common nephropathy in adults after focal segmental glomerulosclerosis.
- MN is a rare disease with a highly variable prognosis. The course of the disease ranges from spontaneous remission to persistent proteinuria or end-stage renal disease (ESRD) making the burden of disease challenging to characterize.
- The objective of this study was to characterize and highlight the disease burden of MN including epidemiology, clinical, humanistic, and economic outcomes, and identify unmet needs and gaps in current knowledge.

Methods

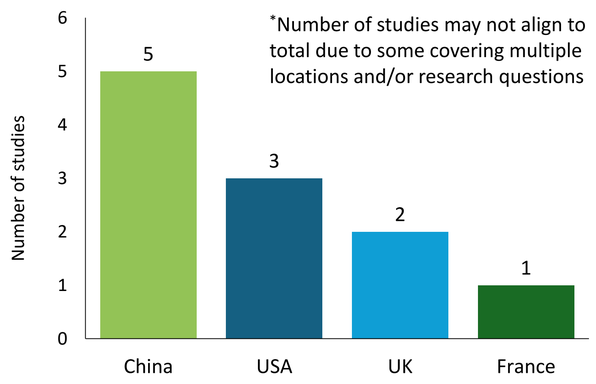
- A targeted review and synthesis of the current literature on epidemiology, clinical, economic, and humanistic burden was conducted to identify relevant articles published between January 2013 and August 2023 in the following scope markets: the US, the UK, Germany, France, China, and Japan. Searches on clinical guidelines, randomized controlled trials related to standard of care, and health technology assessment outcomes were also conducted to understand the landscape situation in MN.

Results

1. The analysis of incidence rates indicates that MN qualifies as a rare disease.

- In total, 10 relevant studies reporting on the epidemiology in patients with MN were identified, of which two were disease review studies.[1-10]
- Four retrospective cohort studies reported results by PLA2R biomarker status, of which one study was from the UK and the remaining three were from China.[1-4]
- Most patients with MN are adults. The mean age ranged from 45 years to 58.3 years across studies. Only one study included epidemiology for pediatric patients.[9]

Analysis of geographical location of studies included*:



Based on one of the disease reviews included in scope, the **incidence** of MN was noted[10]:

10-12 per million

2-17 per million

Based on a study in central China, the **prevalence** of MN was noted to have increased significantly[9]:

From **~16%** in the 2009-2013 period → To **~31%** in the 2014-2018 period

- Based on a UK study, MN is not a leading diagnosis among patients who receive a renal transplant, with only 3.9% of transplant recipients being diagnosed with the condition.[8]

- Proportion of patients with **PLA2RAb positive** status among the publications who reported the value ranged from **59.6% to 80%.**[1-4]
- The disease review notes that **antibodies against PLA2R are found in ~70% of adult patients** with the disease and are increasingly being considered a prognostic biomarker.[10]

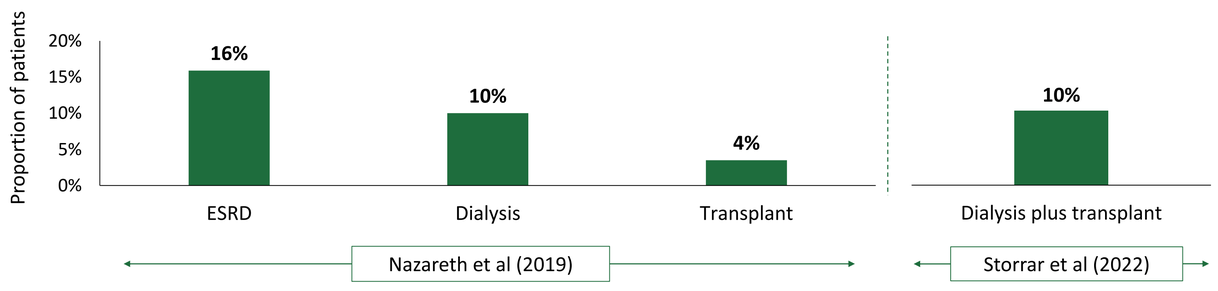
2. Patients with MN have variable treatment patterns and are at risk of developing severe long-term renal complications.

- In total, seven relevant studies were identified reporting on clinical burden in patients with MN. Most studies reported data on ESRD and/or graft failure rates.[1-7]
- Four retrospective cohort studies reported results by PLA2R biomarker status, of which one study was from the UK and the remaining three were from China.[1-3, 7]
- No treatment pattern by line of therapy was identified. Treatment patterns in studies reported from China differed from those in the US, with the most common treatments being cyclophosphamide versus corticosteroids, respectively.[2, 3, 6]

- **43% to 81%** of all patients with MN receive immunosuppressant therapy[1-3, 7]
- **Larger proportion of PLA2R positive patients** receive immunosuppressive treatment, likely due to poorer prognosis expected in this patient group[1-4]

- Two studies reported on the proportions of patients who progress to ESRD, receive dialysis, or undergo renal transplant[1, 7]:

Analysis of proportion of patients with MN who have ESRD, receive dialysis, or undergo renal transplantation[1-2]:



Among transplant patients, **graft failure and mortality rates** were **20%** and **16%,** respectively.[5, 7]

ESRD dialysis and **graft outcomes** were **not studied by PLA2R status** in the included studies. Patients who were **PLA2R—experienced a higher CR rate than PLA2R+ patients**. Association between PLA2RAb and clinical remission remains uncertain.

3. There is an absence of comprehensive economic data across markets, which hinders the ability to accurately characterize the economic burden of MN.

- Only one US retrospective observational analysis that studied commercially insured patients with MN was identified to report resource use and costs grading[7]:

Highest cost → Outpatient costs → In-patient care and services → Prescription-related costs → **Lowest cost**

4. Although few patients with MN receive a transplant, a larger number of patients are likely to develop ESRD, requiring dialysis support. ESRD has a considerable impact on patients:

Humanistic burden

- **Physical** symptoms, **emotional** stress, and overall **diminishing of daily function** from dialysis[10-12]
- The **humanistic burden** of disease is **largely uncharacterized**. A lack of HRQoL data is likely to be a major **limitation for the payers**

Economic burden

- High cost of treatment is largely **driven by the utilization of ESRD facilities** (under out-patient costs) and in-patient visits
- The absence of comprehensive economic data across markets **hinders the ability to accurately understand the burden**

5. Gap analysis

Epidemiology	NA	• Regional incidence for US and EU • Prevalence in China	• Japan • Asian (regional) • European (regional) • Global
Clinical burden	NA	• Available treatments • Proportion of patients progressing to ESRD • Patient mortality rate • Graft failure rate	• Survival rates • Hospitalization rates • Pediatric survival/mortality
Humanistic burden	NA	NA	• Physical symptoms • Emotional impact • Quality of life
Economic burden	NA	• Total resource use • Pharmacy costs	• Direct costs • Indirect costs

High data availability | Moderate data availability | No data available

Conclusions

- The burden of disease revolves around ESRD as an outcome, likely being a major driver for both the costs of MN and its impact on the patient's quality of life.
- Establishing a relationship between biomarkers and long-term outcomes may be leveraged with payers in the future, if such biomarkers become validated in the relevant population.
- The absence of approved treatments alongside some notable gaps in data, particularly in the humanistic and economic impact of MN, suggests that the value of new treatments in this disease area may be underestimated and emphasizes the need for additional research to better inform treatment strategies and support payer decisions.

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Abbreviations: CR, complete response; ESRD, end-stage renal disease; MN, membranous nephropathy; pMN, primary MN; sMN, secondary MN; UK, United Kingdom; US, United States.

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