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Characterizing the burden and unmet need of antibody-mediated rejection

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Introduction and objectives

- Antibody-mediated rejection (AMR) is a significant complication after kidney transplantation and is recognized as a major cause of acute and chronic kidney allograft dysfunction with an eventual progression to allograft failure.
- Active AMR refers to the rapid and severe rejection of transplanted organ, occurring within the first few weeks after transplantation. Chronic active AMR is a subset of AMR, characterized by the presence of circulating donor specific antibodies (DSAs), and histopathologically, it is a chronic allograft injury.
- The burden of AMR is largely uncharacterized, meaning payers and healthcare providers may fail to appreciate the economic and humanistic value of new AMR treatments.
- The objective of this study was to highlight the disease burden of AMR, including epidemiology, clinical, humanistic, and economic outcomes, and identify the 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 (HTA) outcomes were also conducted to understand the landscape situation in AMR.

Results

1. About 1 in 10 kidney transplant results in AMR.

- In total, seven relevant studies reporting on the epidemiology (ie, proportion of transplant patients with AMR, incidence and prevalence rates in general population) in patients with AMR were identified. The studies consisted of three prospective cohort studies, three retrospective studies, and one literature review.[1-7]
- Geographical distribution of the studies:

- The sample size of the seven studies differed greatly, ranging from 46 to 5,679 patients.[1-7]
- Data from 2 additional studies[8, 9] were included because of their relevance for epidemiology data, but these studies were not included in the exclusion criteria (one study was from Switzerland[8] and the other was an Expert Consensus From the Transplantation Society Working Group[9]).

The percentage of kidney transplants resulting in **AMR** ranged from[2-8]:

20% to 38%

The percentage of kidney transplants resulting in **chronic AMR** ranged from[9]:

7.5% to 20.1%

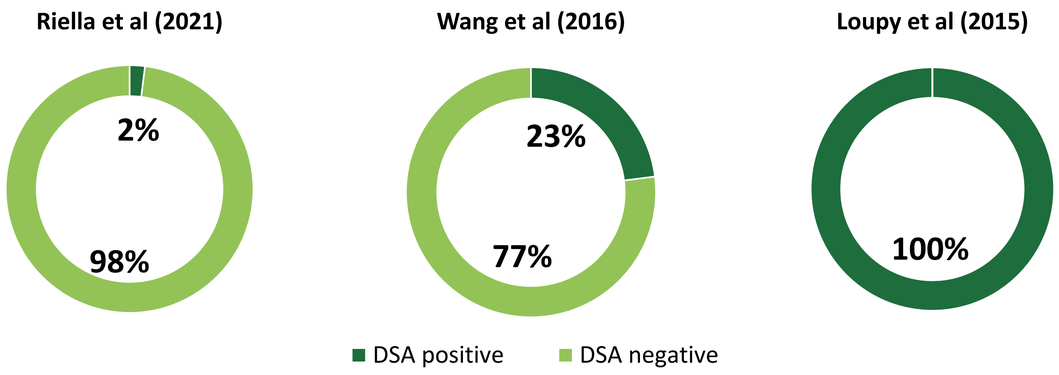
The **mean age** across four studies ranged from[2-4, 7]:

42 to 51 years

2. In patients with AMR, 8-year graft survival is only 56%.[4]

- It is not clear what percentage of patients with AMR have **DSAs.** The percentage ranged from **2% to 100%** across the three studies identified.[1, 4, 5]
- **Graft loss in the 2 years after transplant is 10 times higher in DSA positive patients** (15%) than in DSA negative patients (1.5%).[5]
- Antibody-targeting therapy can **reduce graft failure by 10%.**[4]

Analysis of the presence of DSAs in patients diagnosed with AMR[1, 4, 5]:



- Only one study reported on treatment patterns for patients with AMR, highlighting the patient distribution per baseline therapy[7]:

73.9% of patients with AMR received plasmapheresis (PP)

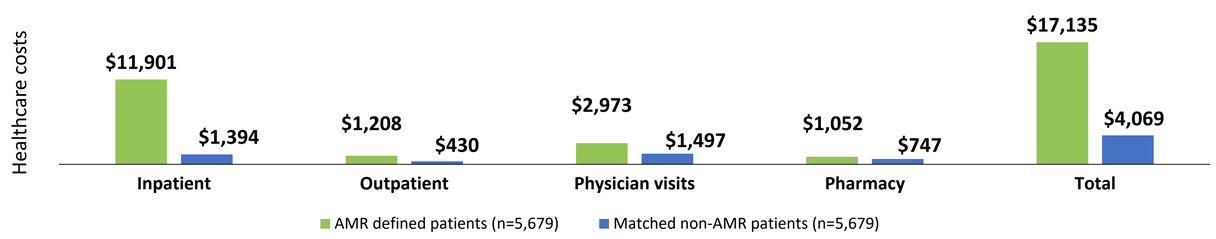
26.1% of patients with AMR used intravenous immunoglobulin (IVIG) in combination with PP

17.4% of patients with AMR used IVIG in combination with rituximab (RTX)

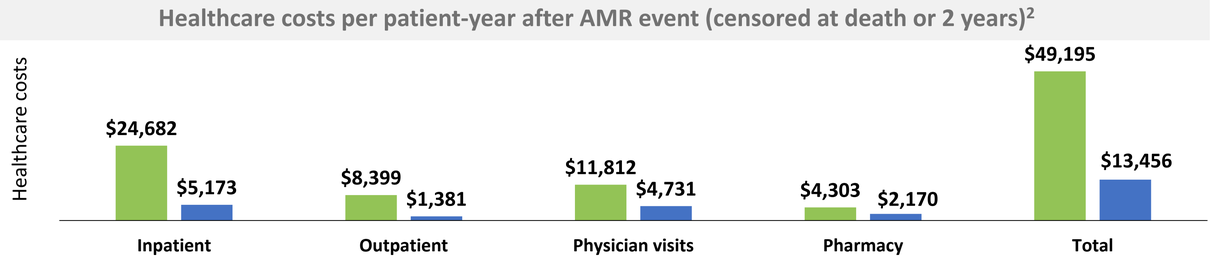
3. Cost data is very limited, but the total additional hospital cost of a patient with AMR in the US is $44,645.[6]

- In the US, the total additional hospital cost for a patient with AMR is $44,645.[6]
- The total additional US healthcare cost per patient 60 days before an AMR event is $13,066 and $35,739 per year after an AMR event, which is mainly driven by in-patient visits.[2]

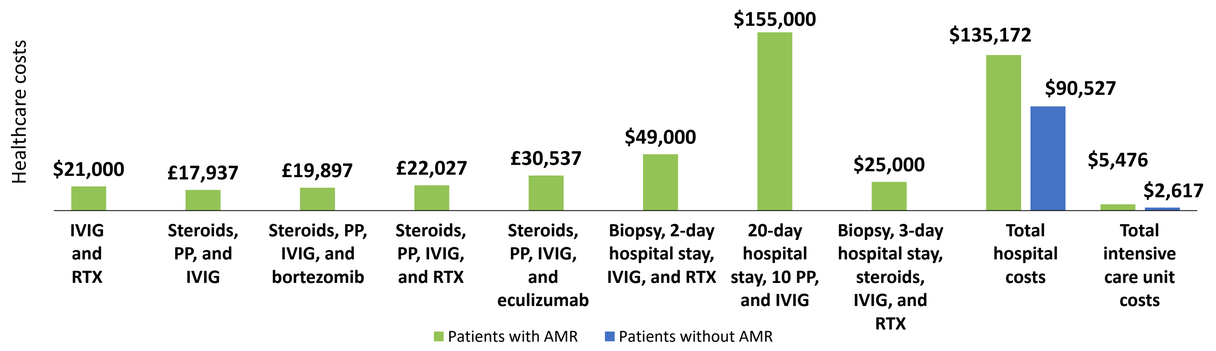
Healthcare costs per patient up to 60 days before AMR event[2]



Healthcare costs per patient-year after AMR event (censored at death or 2 years)[2]



Costs associated with the treatment of AMR in renal transplant recipients.[2]
Number of doses per sessions per treatment omitted for conciseness



4. There are no HRQoL data available for patients with AMR.

- No data on HRQoL for patients with AMR could be found across all markets.[1-7]
- One study showed how all patients with AMR experience microcirculation inflammation and over 50% experience moderate to severe arteriosclerosis.[4]

5. Gap analysis

Epidemiology	USA	• China • Germany • France • UK	• Japan • Asian (regional) • European (regional) • Global
Clinical burden	NA	• Graft survival/loss • Patient survival/mortality • Hospitalization rates	• Pediatric survival/mortality
Humanistic burden	NA	NA	• Physical symptoms • Emotional impact • Quality of life
Economic burden	NA	• Total hospitalization costs • Direct costs • Pharmacy costs	• Indirect costs

High data availability | Moderate data availability | No data available

Conclusions

- The percentage of patients with AMR who had graft failure varied a lot between the studies identified, which makes efforts to characterize the extent of the clinical burden highly uncertain.
- The lack of HRQoL data for AMR across all markets means it will be difficult for HTA agencies and payers to assess the humanistic value of new treatments for AMR.
- The limited cost data outside the US will create a challenge for payers to assess the cost-effectiveness and budget impact of new treatments for AMR.

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Abbreviations: AMR, antibody-mediated rejection; DSA, donor specific antibody**;** HRQoL, health-related quality of life; HTA, health technology assessment; IVIG, intravenous immunoglobulin; PP, plasmapheresis; RTX, rituximab; UK, United Kingdom; US, United States.

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