EPH232: The disease burden and healthcare resource utilization of gram-negative multi-drug resistant bacteria

Jennifer Young[1], Scarlette Pacis[1], Anna Bolzani[1], Thomas Wilke[2], Andrea Fuchs[3]
[1]Cytel, Inc., Berlin, Germany, [2]IPAM, Wismar, Germany, [3]AOK PLUS, Dresden, Germany[3]

While a reduction in annual prevalence of gram-negative MDR indicates efforts implemented to reduce resistance may have a positive impact, mortality rates of these patients are still high, emphasizing the need for more anti-microbial resistant antibiotics.

Background

- In 2019, the Robert Koch Institute reported 9,650 deaths attributable to AMR (mortality rate: 5 per 100,000) and 45,700 deaths associated with AMR (mortality rate: 22 per 100,000) in Germany alone (RKI, 2022).[1]
- WHO considers anti-microbial resistance a global health threat and has listed gram-negative multi-drug resistant (MDR) bacteria as priority pathogens (WHO, 2021).[2]
- These have been linked to hospital-acquired infections, such as bloodstream infections and pneumonia (Mancuso et al., 2021).[3]
- Due to risk factors such as comorbidities, elderly patients are most at risk of acquiring hospital-related infections associated with gram-negative MDR (Claudia et al., 2013).
- Thus, this study aimed to evaluate the disease burden and healthcare resource utilization (HCRU) of gram-negative MDR bacteria in the elderly population in Germany

Objective

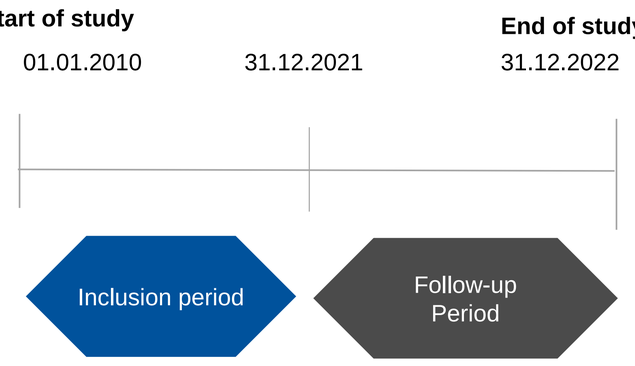
- Analyze AOK plus claims data and estimate the annual prevalence number of elderly patients (>65) who acquired gram-negative multi-drug resistant bacteria as a secondary infection while hospitalized.
- Calculate the number and length of disease-related hospitalizations of patients with gram-negative MDR bacteria (ICD-10-GM: U81!)
- Estimate the average hospitalization length and mortality rate.

Methods

Data

- This retrospective analysis was based on anonymized claims data of a German sickness fund (AOK PLUS)
- Patients included were ≥65 years and had at least one inpatient diagnosis of gram-negative MDR bacteria (ICD-10-GM: U81!) and were observed between January 01, 2010 and December 31st, 2021 with an index date defined as the first diagnosis (Figure 1).
- Patients were followed up for one year after index date (until December 31st, 2022).

Figure 1. Study overview



Analysis

- Descriptive analysis included patient demographics, the average length of hospitalization, and the main diagnosis code recorded at index date.
- The frequency and average length of all-cause hospitalization were determined for one-year follow-up
- Patient mortality at 3/6/9/12 months after index was calculated using Kaplan-Meier methodology.
- The annual prevalence of MDR among all hospitalizations for patients aged ≥65 was estimated for each year of 2017 to 2021.
- Patients were divided into groups based on age:
  - Group 1: 65-80
  - Group 2: Over 80
- Two sample-tests were applied to investigate if there were any significant differences observed between each group for the following outcomes: mean CCI, mean index hospitalization length, HCRU outcomes after one year follow-up and mortality

Results

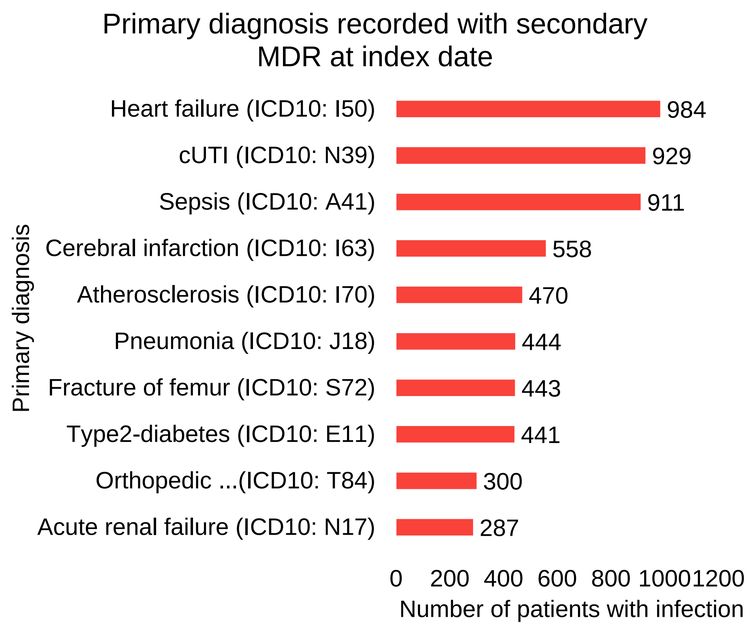
Results recorded at index date

- A total of 18,058 patients with an inpatient diagnosis of gram-negative MDR were identified (female: 52%, mean age: 80 years, mean CCI: 4.0, average index hospitalization length: 21 days). The results recorded for each group are shown in Table 1.
- Heart failure (ICD-10: I50, n= 984), complicated urinary tract infection (cUTI) (ICD-10: N39, n= 929) and sepsis (ICD-10: A41, n= 911) were the most common reasons for hospitalization (Figure 2).

Table 1. Baseline characteristics and comorbidity recorded at index date

Baseline factors	Group 1: 65-80	Group 2: Over 80	P-value
Total patients, n (%)	9,487 (52.5%)	8,571 (47.5%)	-
Age, mean (SD), years	73.6 (4.7)	86.3 (4.1)	P < 0.001
Female, n (%)	3,989 (42.0)	5,317 (62.0)	P < 0.001
Mean CCI (sd)	4.0 (2.8)	3.9 (2.4)	P < 0.001
Mean index hospitalization length (sd)	25 (26.4) days	17 (17.0) days	P < 0.001

Figure 2. Top 10 primary diagnosis present when secondary gram-negative MDR was recorded at index date



Results recorded during one-year follow-up

- During the one-year follow-up, patients experienced an average frequency rate of 1-2 hospitalizations (all-cause), and the mean length of hospital stay was 20 days for Group 1: 65-80 and 12 days for Group 2: Over 80 (Table 2).
- The annual prevalence of gram-negative MDR bacteria in the elderly population has decreased by almost 50% from 2017 (1.73%) to 2021 (0.90%) (Figure 3).
- For all patients, patient mortality at 3/6/9/12 months after index date was 26%/35%/40%/44%, respectively.
- Patient mortality rates increased by each time point in both groups (Figure 4).

Table 2. HCRU after one year follow-up

Baseline factors	Group 1: 65-80	Group 2: Over 80	P-value
Mean frequency of all-cause hospitalizations, mean (sd)	1.9 (2.4)	1.3 (1.8)	P < 0.001
Mean days hospital length, mean (sd)	20.4 (31.9) days	11.9 (19.6) days	P < 0.001

Figure 3. Annual prevalence of gram-negative MDR

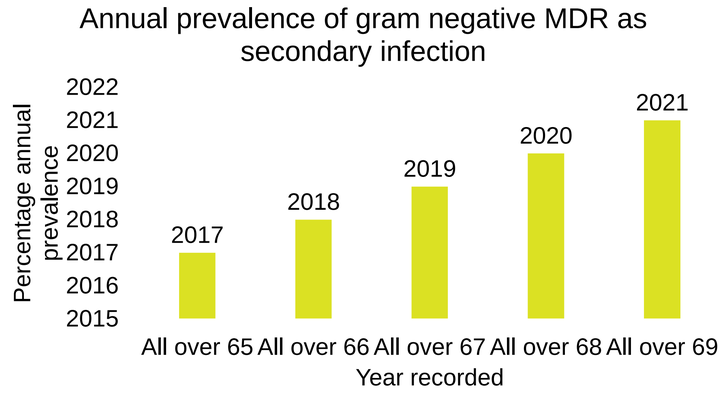
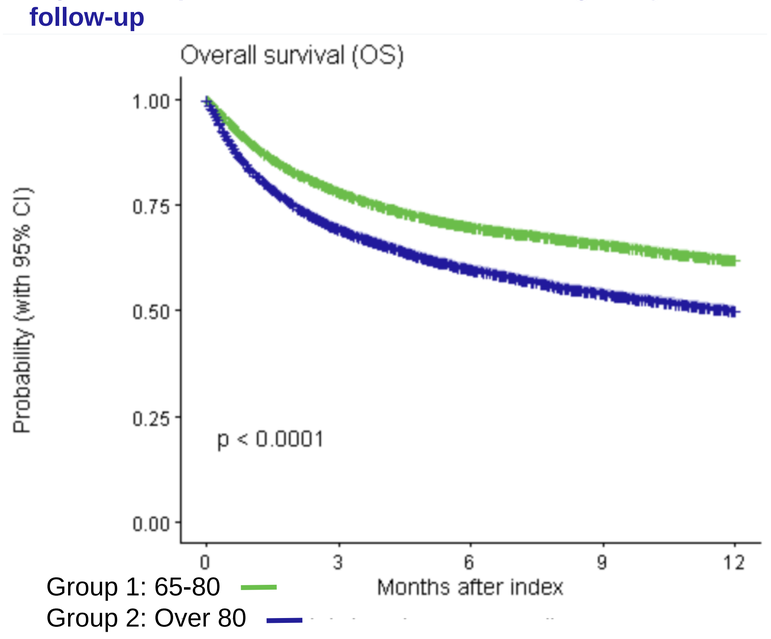


Figure 4. Kaplan Meier overall survival during one year follow-up



Group	Number at risk (number censored)				
Group 1: 65-80	9,487 (2)	7,236 (209)	6,270 (416)	5,716 (602)	0 (6000)
Group 2: Over 80	8,571 (2)	5,809 (169)	4,857 (331)	4,269 (460)	0 (4411)
Timepoint (months)	0	3	6	9	12

Differences recorded between age groups

- Age groups in the elderly played a significant role in differences between HCRU outcomes and mortality
  - Mean CCI and mean index hospitalization length were significantly more for Group 1: 65-80 (Table 1)
  - Mean frequency of all-cause hospitalizations recorded and mean days in hospital length were also significantly more for Group 1: 65-80 (Table 2)
  - Mortality rates in Group 2: Over 80 were higher compared to Group 1: 65-80

Conclusion

- The study revealed a decline in the annual prevalence of gram-negative MDR infections in all age groups while observing high mortality rates throughout the one-year follow-up period.
- Patients aged 65-80 exhibited greater HCRU outcomes than patients over 80 who had higher mortality rates.

Abbreviations

AMR: Antimicrobial Resistance; AOK Plus: Die Gesundheitskasse für Sachsen und Thüringen; CCI: Charles Comorbidity Index; cUTI: complicated Urinary Tract Infection; HCRU: Healthcare Resource Use; MDR: Multi Drug Resistance; WHO: World Health Organization

References

1. The burden of antimicrobial resistance in G7 countries and globally: AN URGENT CALL FOR ACTION, 2022. Accessible here [https://www.rki.de/EN/Content/infections/antibiotic/brochure_IHME_RKI.pdf?__blob=publicationFile]. 2. WHO, 2022. Accessed here [https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance], 3. Mancuso G, Midiri A, Gerace E, Biondo C. Bacterial Antibiotic Resistance: The Most Critical Pathogens. Pathogens. 2021 Oct 12;10(10):1310. doi: 10.3390/pathogens10101310. PMID: 34684258; PMCID: PMC8541462., 4. Claudia M. Denkinger, Alison D. Grant, Michael Denkinger, Shiva Gautam, Erika M.C. D'Agata, Increased multi-drug resistance among the elderly on admission to the hospital—A 12-year surveillance study, Archives of Gerontology and Geriatrics, Volume 56, Issue 1, 2013, Pages 227-230, ISSN 0167-4943,

Disclosures

- The study conducted did not receive sponsorship and none of the authors involved have conflicts of interest.

Presented at ISPOR EU | Copenhagen, Denmark | November 12–15, 2023

Contact information: www.cytel.com