

# FEASIBILITY OF EVALUATING THE BURDEN OF $\beta$ -THALASSEMIA WITH GERMAN CLAIMS DATA

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## BACKGROUND

- $\beta$ -thalassemia is an inherited genetic disease characterized by reduced or absent production of functional  $\beta$ -globin, resulting in an impaired development and survival of red blood cells (RBCs) and leading to chronic anemia and other serious complications.<sup>1</sup>
- Patients with severe  $\beta$ -thalassemia require regular blood transfusions and treatment for iron overload to survive while patients with minor forms may not experience any symptoms.<sup>2,3</sup>
- The incidence and prevalence of  $\beta$ -thalassemia differs according to geographic location, with endemic populations primarily found in South Asia, the Middle East, North Africa, and Southern Europe.<sup>4</sup>
- While migration is spreading the global distribution of the disease, in most European countries as well as the United States  $\beta$ -thalassemia still is a rare disease.<sup>5</sup>
- The prevalence of  $\beta$ -thalassemia in Germany and its burden to patients and the German healthcare system has not yet been systematically assessed.

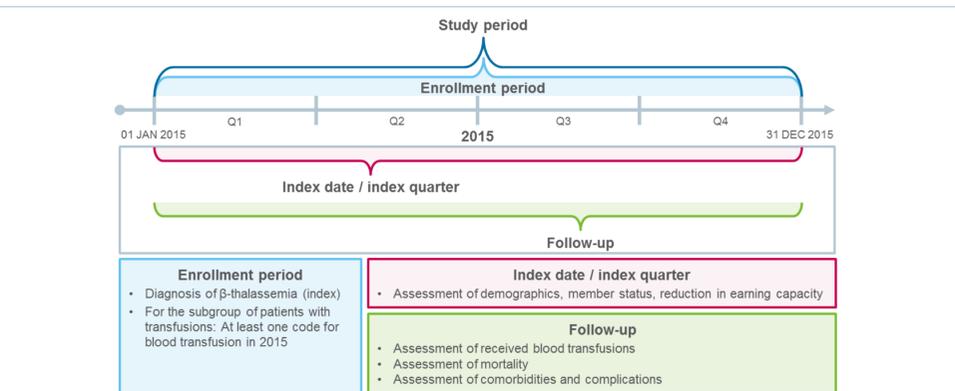
## OBJECTIVE

- The aim of the study was to assess the prevalence of  $\beta$ -thalassemia in Germany and to evaluate its burden to patients and the healthcare system.

## METHODS

- A retrospective claims database analysis was conducted using the "Institut für angewandte Gesundheitsforschung Berlin" (InGef) research database.
- The database comprises anonymized healthcare claims of about 4 million covered lives insured in the Statutory Health Insurance (SHI) in Germany.
- This sample represents about 4.8% of the German population and 5.6% of the German SHI population and is structured to represent the German population in terms of age and gender.
- The InGef research database was proven to have good external validity to the German population in terms of morbidity, mortality, and drug use.<sup>6</sup>
- Prevalent  $\beta$ -thalassemia patients within the database were identified retrospectively between January 1<sup>st</sup>, 2015 and December 31<sup>st</sup>, 2015 using the International Statistical Classification of Diseases and Related Health Problems, 10<sup>th</sup> revision, German Modification (ICD-10-GM) code D56.1 "Beta-Thalassemia" in the outpatient sector (verified diagnoses) or in the inpatient sector (primary or secondary diagnosis).
- Individuals who died in the study timeframe were not excluded from the analysis.
- The proportion of prevalent  $\beta$ -thalassemia patients receiving blood transfusions was determined by Operation and Procedure Codes (OPS) for blood transfusions in the inpatient setting and Pharmaceutical Registration Numbers (PZN) for blood products in the outpatient setting, namely erythrocyte concentrate and whole blood. Categories of the number of received blood transfusions were pre-defined as "0 blood transfusion", "1-7 blood transfusions", and "≥8 blood transfusions".
- Study outcomes of interest were the prevalence of  $\beta$ -thalassemia as well as demographic characteristics, member status and reduction in earning capacity, and mortality of identified  $\beta$ -thalassemia patients in 2015. Demographics were determined in terms of age and gender; age was calculated based on the year of birth. The member status of the health insurance was stratified by family insurance, pensioner, full member, and unknown status. Pensioners were further analyzed in terms of age (<60 and <45 years) and whether they were retired due to reduced ability to work.
- Furthermore, the most frequent comorbidities based on ICD-10-GM code groups on a 3-digit level, relevant disease-related complications, and the number of received RBC transfusions were assessed for the year 2015.

Figure 1: Study period and study outcomes

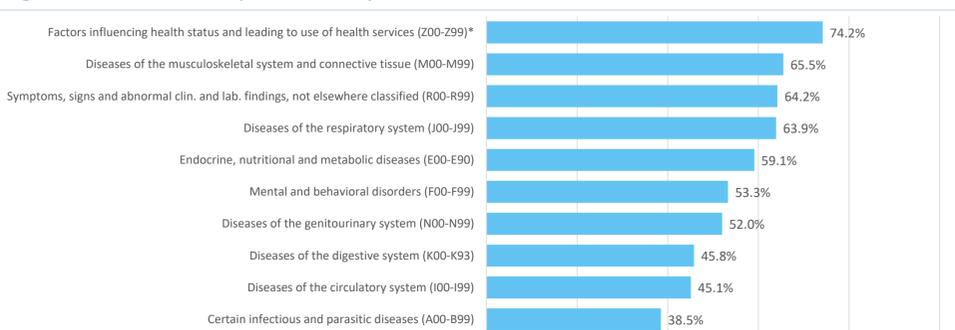


- Patient numbers from the sample of the InGef research database, which is already adjusted for age and gender distribution of the German population, were extrapolated to the underlying German population at December 31<sup>st</sup>, 2015 according to the Federal Office of Statistics (DESTATIS)<sup>7</sup>. Therefore, the number of identified  $\beta$ -thalassemia patients was multiplied by the underlying German population and divided by the underlying sample in the database in 2015. Confidence intervals (CI) with 95% confidence level were calculated by applying the Clopper-Pearson-Interval.

## RESULTS

- A total of 623  $\beta$ -thalassemia patients were identified in the InGef database in 2015.
- The mean age of the patients was 42 years, spanning from 1 to 88 years and 53.0% of the identified  $\beta$ -thalassemia patients were female.
- The two most frequently coded comorbidities of  $\beta$ -thalassemia patients in 2015 were ICD-10-GM code group Z00-Z99 "Factors influencing health status and leading to use of health services" including examination and clarification, followed by the group M00-M99 "Diseases of the musculoskeletal system and connective tissue".
- Moreover, a noticeable amount of  $\beta$ -thalassemia patients (53.3%) had diagnoses of mental and behavioral disorders (F00-F99) in 2015 (see Figure 2).
- The most common disease-specific complications were observed to be diabetes mellitus and heart failure in 17.7% and 5.3% of patients, respectively.

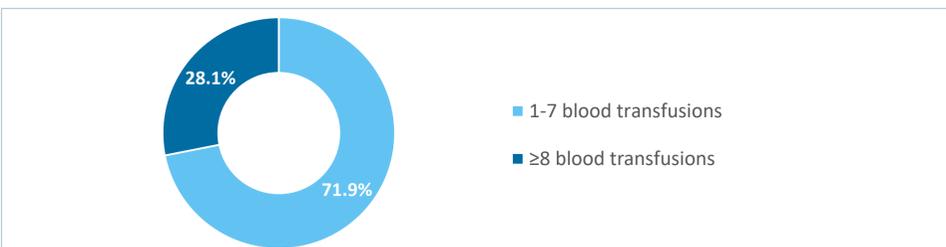
Figure 2: Comorbidities of  $\beta$ -thalassemia patients



\* Z codes include codes for examination and clarification (e.g. check-ups), potential health risks concerning transmissible diseases (e.g. exposure of rabies), reproduction, prophylactic immunization or council for problems not being related to a disease or impairment.

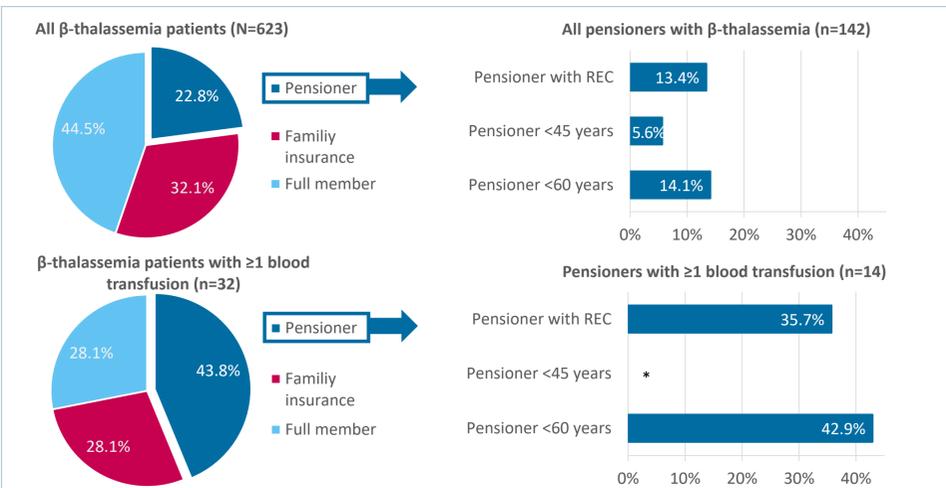
- Of the total sample, 94.9% (n=591) of patients received no RBC transfusions in 2015. The remaining 32 patients had at least one RBC transfusion in 2015.
- Stratified by the number of transfusions, 71.9% (n=23) had 1-7 RBC transfusions and 28.1% (n=9) required ≥8 transfusions (see Figure 3). A mean of 7 transfusions and a maximum of 24 transfusions was observed for the transfused patients.
- The majority of all RBC transfusions (N=210) in 2015 was administered in the outpatient setting (71.0%) and 29.0% were given during inpatient stays in a hospital.

Figure 3: Blood transfusions in  $\beta$ -thalassemia patients in 2015 (n=32)



- Of all  $\beta$ -thalassemia patients, about 44.5% were full members of the SHI, 32.1% were family insured, and 22.8% were pensioners. In the subgroup of  $\beta$ -thalassemia patients with transfusions, most of the patients were pensioners (43.8%) and only 28.1% were full members and family insured, respectively.
- Reduction in earning capacity was observed in 13.4% of all pensioners with  $\beta$ -thalassemia compared to 35.7% of pensioners who received ≥1 blood transfusion (see Figure 4).

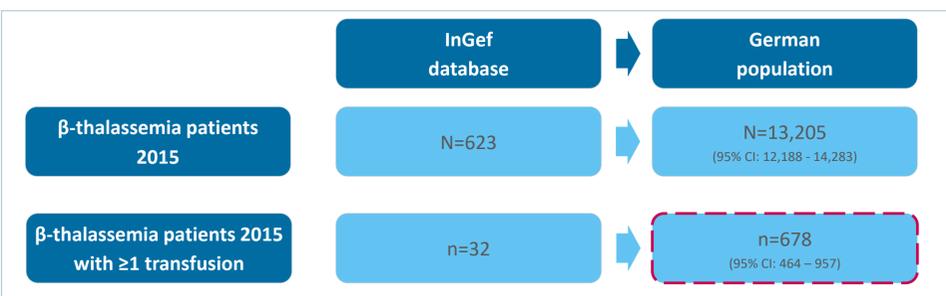
Figure 4: Member status, early retirement and reduction in earning capacity (REC) of  $\beta$ -thalassemia patients in 2015



\* Due to data protection regulations, the proportion of pensioners <45 years could not be reported for the group of  $\beta$ -thalassemia patients with ≥1 blood transfusion (patient count <5).

- The mortality rate in 2015 was noticeably higher in the group of transfused  $\beta$ -thalassemia patients compared to all  $\beta$ -thalassemia patients (18.8% vs. 1.6%).
- Extrapolated to the German population in 2015, about 13,205 patients (95% CI 12,188-14,283) suffered from  $\beta$ -thalassemia and about 678 patients received blood transfusions (95% CI 464-957). This corresponds to a ratio of 16/100,000 persons with  $\beta$ -thalassemia and 0.8/100,000 persons with  $\beta$ -thalassemia on transfusions in Germany (see Figure 5).

Figure 5: Extrapolation of identified  $\beta$ -thalassemia patients to the German population in 2015



## CONCLUSIONS

- Claims data analyses can fill in research gaps in rare diseases and provide evidence on epidemiology, patients' characteristics, and healthcare outcomes.
- With about 13,200  $\beta$ -thalassemia patients extrapolated for the German population, the burden of disease for Germany is significant.
- The results suggest that due to a reduction in their earning capacity and a high morbidity and mortality, transfused  $\beta$ -thalassemia patients are especially affected in their daily life.
- A reasonable conclusion is that the burden of disease increases with a rising number of received blood transfusions. Particularly, transfusion dependent  $\beta$ -thalassemia patients require more intensive monitoring and would have a higher impact on the SHI.
- Given the increased immigration to Germany from the Middle-East in recent years, a significant growth in the prevalence of  $\beta$ -thalassemia can be expected for the German healthcare system.
- In general, claims data analyses are subject to limitations as they are primarily collected for accounting purposes, and therefore clinical parameters (e.g. severity grades, laboratory results), dosage and intake of medication, or additional information (e.g. quality of life) are not covered.

## DISCLOSURE

- The analysis was done by Xcenda and supported by bluebird bio Inc.

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