

## Conclusion

- Half of the patients with nonsevere haemophilia A and inhibitors developed high titre inhibitors.
- More than half of the patients (57%) presented with bleeding complications; 46% had changed to a severe phenotype.
- These findings stress the importance of close follow-up after exposure to factor VIII concentrates in patients with nonsevere haemophilia A.

## Objectives

- The aim of current study was to describe the presenting symptoms of inhibitor development in a large unselected cohort of nonsevere haemophilia A patients.
- Inhibitor development in nonsevere haemophilia A (FVIII:C, 2-40 IU/dL) has a heterogenous clinical phenotype, ranging from irrelevant transient inhibitors to high titre neutralizing antibodies with severe bleeding complications.
- Data on inhibitors in nonsevere patients are scarce and selected, favouring those with severe complications.

## Results

- Two third of the inhibitors developed after the year 2000 (*Fig. 1*). Inhibitors developed after a median of 37 years and 28 exposure days (*Fig. 2*).
- Fifty-seven patients (56%) had developed high titre inhibitors (>5 BU/mL).
- More than half of the patients (n=61) had an increased bleeding tendency at presentation with inhibitor (*Fig. 3*).
- In 80 patients (80%) endogenous FVIII:C was decreased to below 5 IU/dL (including 33/44 patients with low titer inhibitors), of whom FVIII:C fell below  $\leq 0.01$  IU/mL in 49 patients (46%).

Fig. 1 Year of inhibitor detection

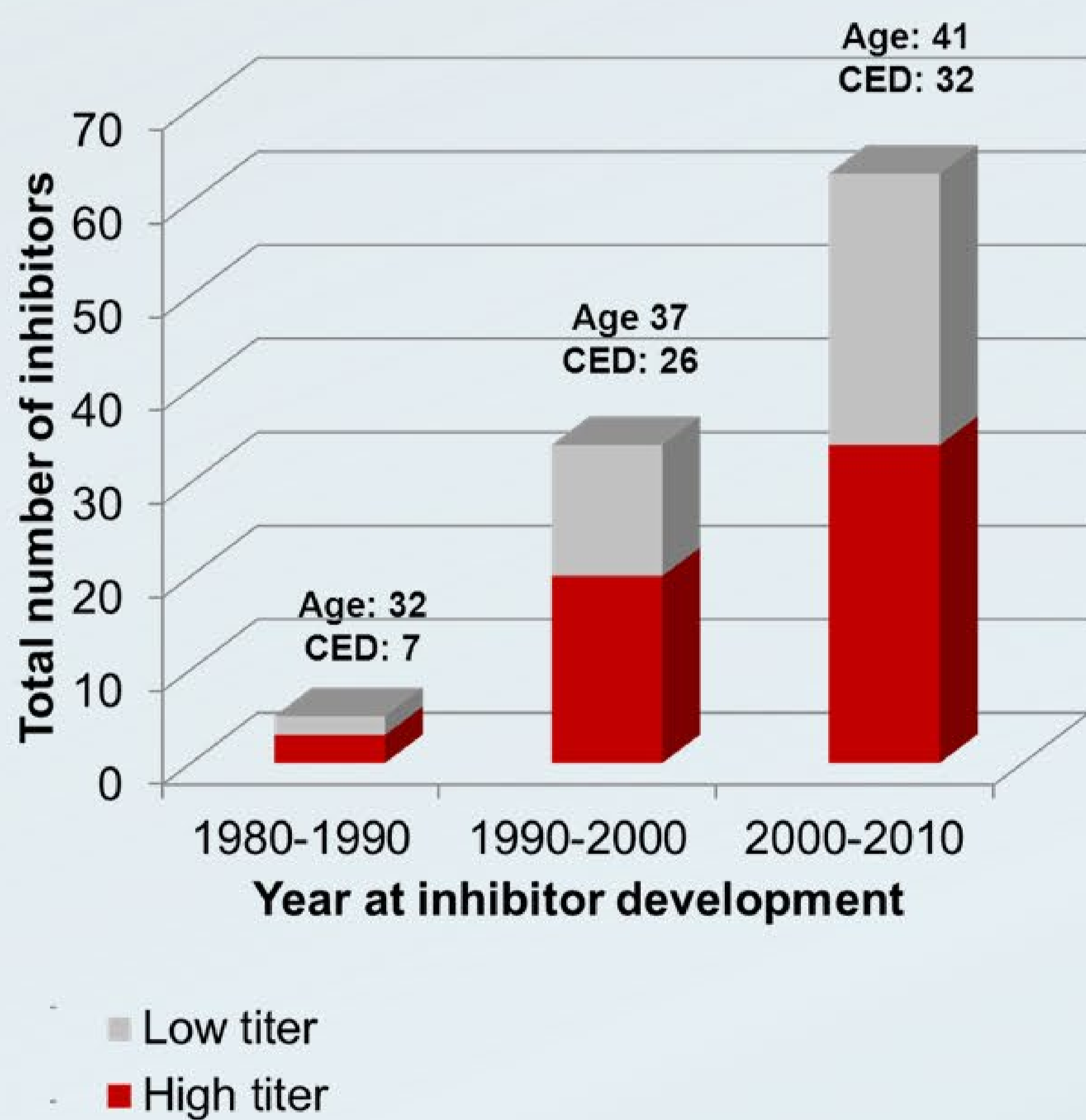


Fig. 2 Age at inhibitor detection

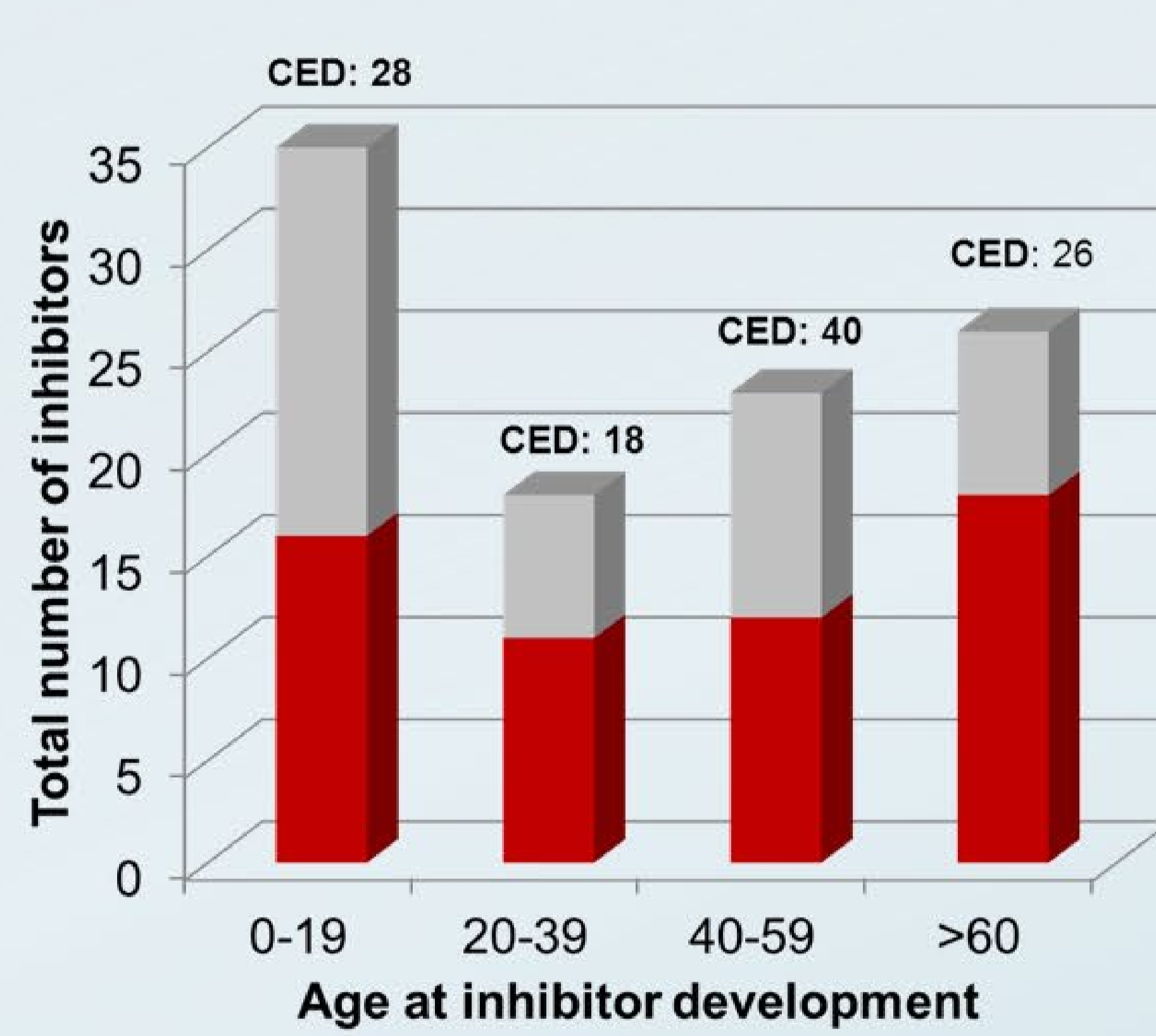
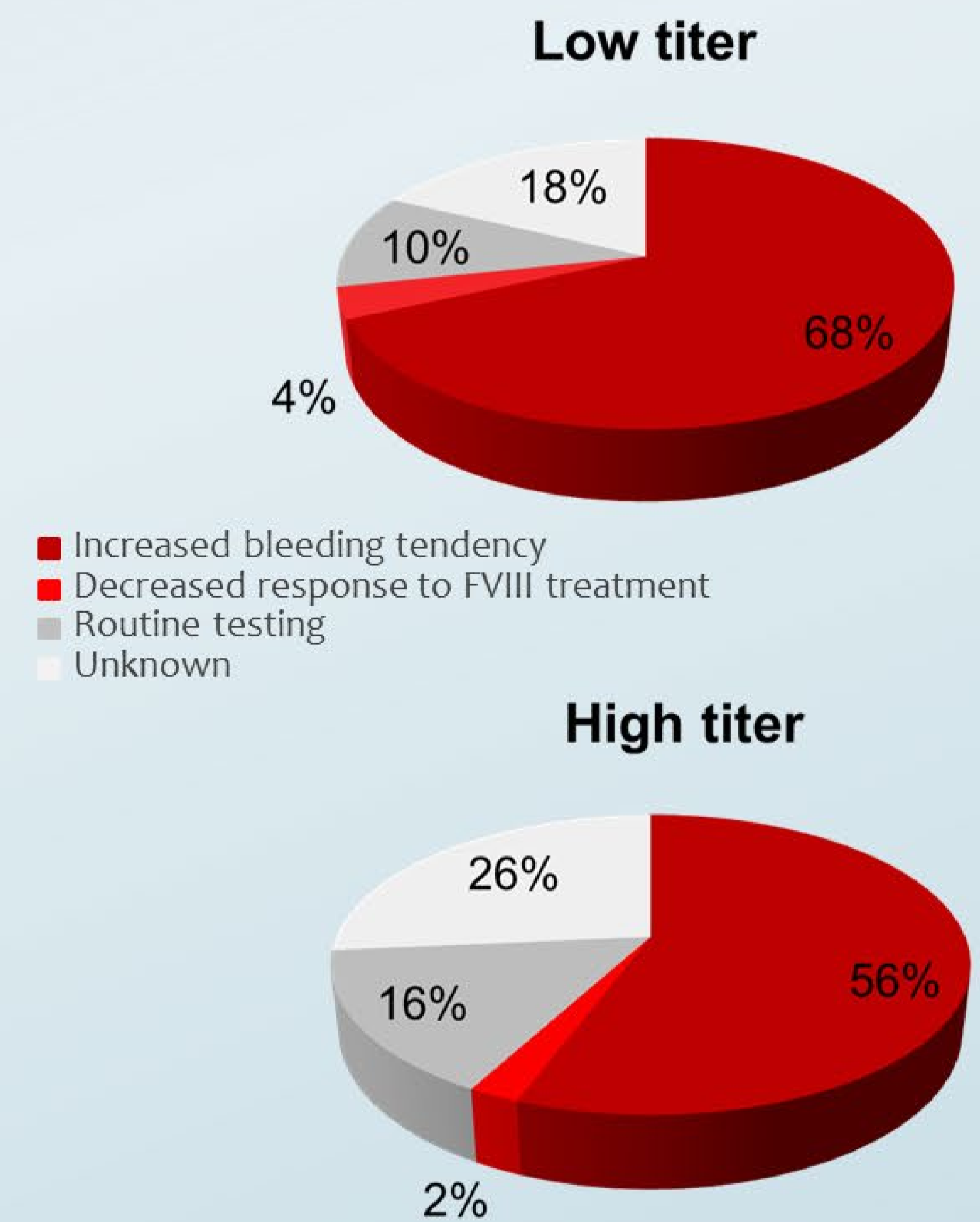


Fig. 3 Reason for inhibitor testing



CED, median cumulative number exposure days to factor VIII; Age, median age in years

## Methods

- Clinical data were collected of 107 inhibitor patients derived from a source population of 2,709 nonsevere haemophilia A patients that were treated between 1980 and 2011 in 34 European and Australian centers.
- Patients were subdivided according to age and calendar period at time of inhibitor development (10-year groups), aiming to search for age-related trends and trends over time.



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