Clinical, humanistic and economic burden in patients with paroxysmal nocturnal haemoglobinuria across the United Kingdom, Germany and France

Insights from the COMMODORE Burden of Illness study

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Introduction

- Paroxysmal nocturnal haemoglobinuria (PNH) is an ultra-rare acquired stem cell disorder, leading to haemolytic anaemia, marrow failure, and thrombophilia[1,2]
  - As a result of these symptoms and complications, health-related quality of life and the ability to work can be impaired[3]
- In the UK, France and Germany, PNH is typically treated with C5 complement inhibitors[4,5], such as eculizumab and ravulizumab
- There is minimal evidence quantifying socio-economic burden of illness in PNH, with only one study published with US data[6]; there are no European data published for people with PNH
- Despite access to treatments, there is a scarcity of literature on remaining unmet needs and costs, warranting the collection of additional data on PNH

1. Parker et al. *Blood*. 2005;106(12):3699–3709
2. Brodsky et al. *Blood*. 2014;124(18):2804–2811
3. Young et al. *Semin Hematol*. 2009;46(1 Suppl 1):S1–S16
4. Devalet et al. *Eur J Haematol*. 2015;95(3):190–198
5. Carreras et al (eds). The EBMT Handbook. Springer International Publishing. 2019;547–556
6. Dingli et al. *Ann Hematol*. 2022;101(2):251–263

PNH, paroxysmal nocturnal haemoglobinuria

Study aims

Primary Objective

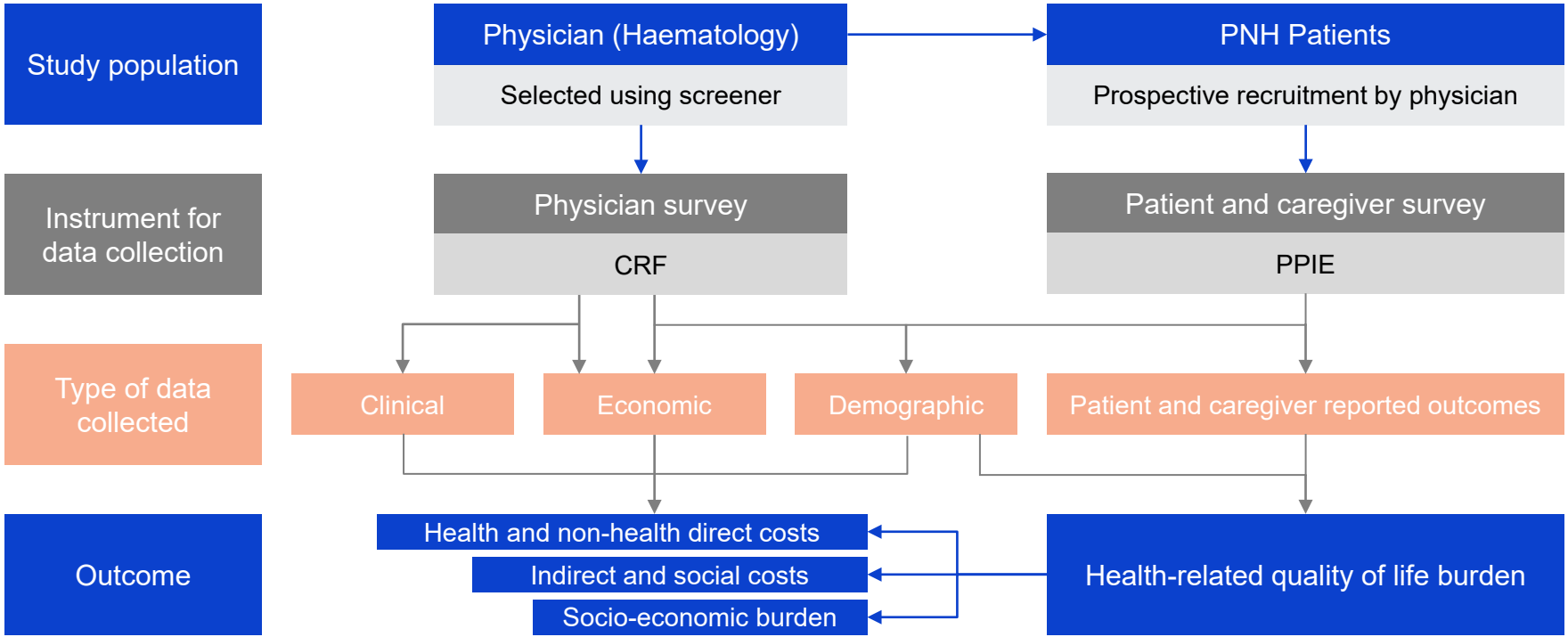
- **Direct medical, direct non-medical and indirect costs associated with PNH at the initial and second index date, to form a longitudinal data analysis**

Secondary Objectives

- **Quality of life**
- **QLQ-AA/PNH-54 questionnaire**

PNH, paroxysmal nocturnal haemoglobinuria; QLQ-AA/PNH, quality of life questionnaire for patients with aplastic anemia and/or paroxysmal nocturnal haemoglobinuria

Schema of the cross-sectional, observational, longitudinal burden of illness study, comprising two phases



CRF, case report form; PNH, paroxysmal nocturnal haemoglobinuria; PPIE, Patient public involvement and engagement form

Methods

- Quality of life was assessed through PRO questionnaires:
  - FACIT-F
  - PGIS
  - QLQ-AA/PNH-54
  - EQ-5D-5L

Cost type	Category
Costs to healthcare system (Source CRF)	Tests and examinations
	Medication
	Consultant visits
	Procedures
	Hospitalisations
Costs to patient (Source PPIEp)	Travel costs
	Alternative therapies
	Professional caregiver
	Work productivity impact patient
Costs to caregiver (Source PPIEc)	Travel costs
	Work productivity impact caregiver

The analysis conducted as part of this study is descriptive, and it is presented across the full first-phase base case sample

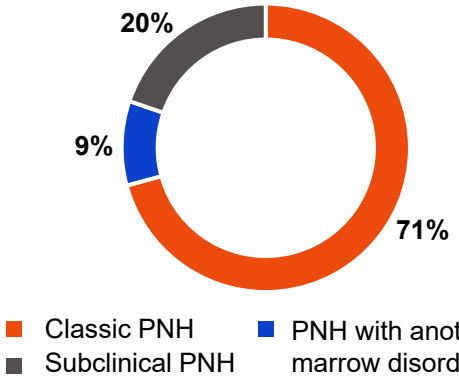
CRF, case report form; EQ5D-5L, EuroQol - 5 dimension 5-level version; FACIT-F, functional assessment of chronic illness therapy – fatigue; PGIS, patient global impression of severity; PNH, paroxysmal nocturnal haemoglobinuria; PPIEc, patient and public involvement and engagement caregiver questionnaire; PPIEp, patient and public involvement and engagement patient questionnaire; PRO, patient-reported outcome; QLQ-AA/PNH, quality-of-life tool for patients with aplastic anaemia and/or PNH

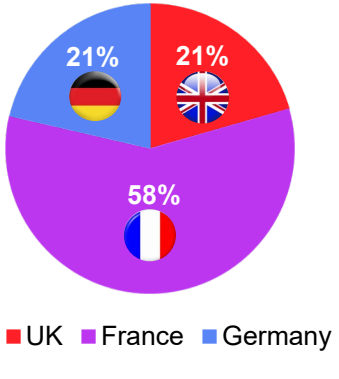
Results: baseline demographic and clinical characteristics (N=243)

- 243 CRFs, 74 participant PPIEs, and 39 caregiver PPIEs were completed
- The mean age was 41.6 years
- The majority of participants were male (64.2%) and white (86.4%)
- Thrombosis events were reported in approximately one third of the sample
- Hemolysis events were reported for more than half of the participants

Reported PNH complications†	Total (n=243)
Thrombosis event reported, n (%)	90 (37.1%)
Haemolysis event reported, n (%)	141 (58.0%)

Complement inhibitors, n (%)	Total (n=243)
Eculizumab	114 (47%)
Ravulizumab	36 (14.8%)
Pegcetacoplan	2 (0.8%)





CRF, case report form; PPIE, patient and public involvement and engagement;
PNH, paroxysmal nocturnal haemoglobinuria; PPIE, patient and public involvement and engagement

†At least 1 thrombotic event and at least 1 haemolysis event

Results: quality-of-life outcomes in 74 patients with available PPIE data

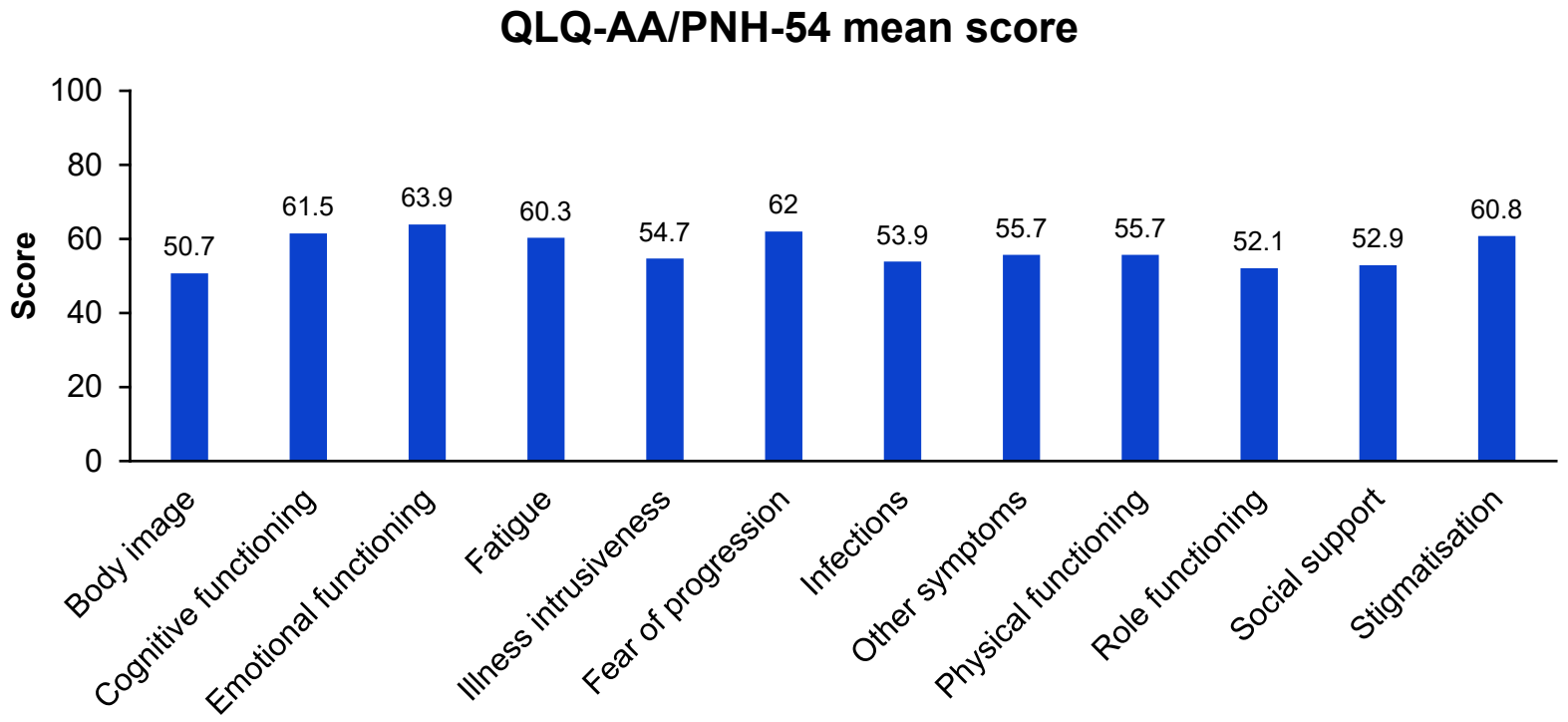
Quality of life and severity of disease measures	Total (n=74)
FACIT-F scale score, mean (SD)	29.9 (7.4)
PGIS score, mean (SD)	4.3 (2.5)
QLQ-AA/PNH-54 emotional functioning score, mean (SD)	63.9 (19.8)
QLQ-AA/PNH-54 fear of progression score, mean (SD)	62.0 (18.1)
QLQ-AA/PNH-54 cognitive functioning score, mean (SD)	61.5 (21.6)
EQ5D-5L index score, mean (SD)	0.84 (0.2)

- The mean FACIT-F score outcome was below 30
- Via the PGIS questionnaire, 25.7% of the sample reported perception of ‘most severe’ symptoms and 25.7% reported perception of ‘moderately severe’ symptoms
- For the QLQ-AA/PNH-54, the highest mean scores were associated with the ‘emotional functioning’, ‘fear of progression’ and ‘cognitive functioning’ components
- The overall EQ-5D mean score was below the normative levels[1]

EQ-5D, EuroQol-5 dimension; FACIT-F, functional assessment of chronic illness therapy – fatigue; PGIS, patient global impression of severity; PNH, paroxysmal nocturnal haemoglobinuria; PPIE, patient and public involvement and engagement; QLQ-AA/PNH, quality-of-life tool for patients with aplastic anaemia and/or PNH; SD, standard deviation

1. Azzi et al. *Value in Health.* 2020; 23(Suppl 2):S685

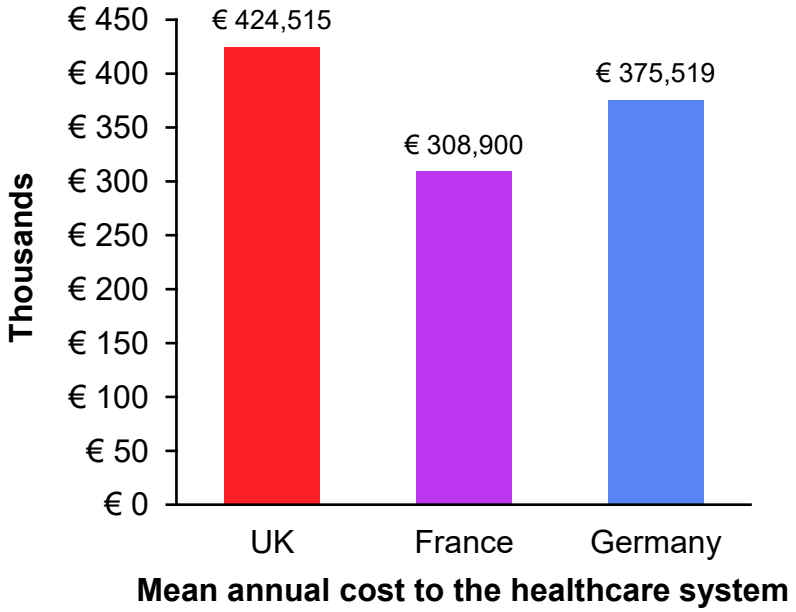
Results: quality-of-life (QLQ-AA/PNH-54) outcomes



PNH, paroxysmal nocturnal haemoglobinuria; QLQ-AA/PNH, quality-of-life tool for patients with aplastic anaemia and/or PNH

Results: cost to the healthcare system via physician and patient/caregiver surveys (N=58)

Mean costs to healthcare system	Total (N=58)
Mean treatment cost†	**€ 330,823**
Mean consultations cost	€ 129
Mean procedures cost	€ 1,964
Mean tests cost	€ 51
Mean hospitalisation cost	**€ 11,880**
Mean costs to healthcare system	**€ 344,848**



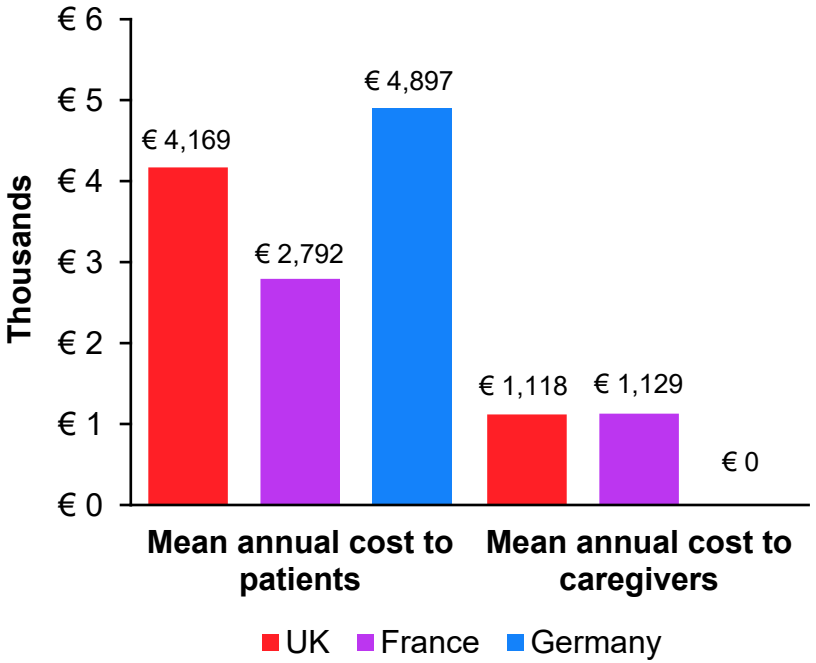
†Treatment cost includes complement inhibition therapy costs

Results: cost to the patients and caregivers

- The main drivers for patient and caregiver costs were travel due to PNH and work loss

Mean annual costs to patients	Total (n=58)
Mean travel cost	€ 1,650
Mean professional caregiver cost	€ 286
Mean alternative therapy cost	€ 13
Mean cost of work loss - patient	**€ 1,432**
Mean costs to patients	**€ 3,379**

Mean annual costs to caregivers	Total (n=58)
Mean travel cost	€ 395
Mean cost of work loss - caregiver	€ 766
Mean costs to caregivers	**€ 990**



PNH, paroxysmal nocturnal haemoglobinuria

Conclusions

- Over two-thirds of the sample was diagnosed with classic PNH, and most of these participants received complement inhibitor therapy in the 12 months prior to enrolment
  - A third of patients had at least one thrombotic event reported in the 12 months prior to enrolment
- The results of the first phase of the study show that PNH has an impact on patients' QoL, as per the FACIT-F results (indicating severe fatigue), as well as EQ-5D (mean utilities below normative values)
  - The subsample, where all costs were available, incurred high costs to the healthcare system
  - Compared to the identified US burden of illness study[1], the European data also shows anaemia and thrombotic outcomes, reported even in the sample treated with C5 inhibitors
  - A significant unmet need is still present in the PNH population

EQ-5D, EuroQol-5 dimension; FACIT-F, functional assessment of chronic illness therapy – fatigue; PNH, paroxysmal nocturnal haemoglobinuria; QoL, quality of life

1. Dingli et al. *Ann Hematol*. 2022;101(2):251–263

Acknowledgments

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Thank you!