X-Linked Hypophosphatemia Registry – an international prospective patient registry

Raja Padidela[1], Ola Nilsson[2], Agnès Linglart[3], Outi Mäkitie[4], Signe Beck-Nielsen[5], Gema Ariceta[6], Dirk Schnabel[7], Maria Luisa Brandi[8], Annemieke Boot[9], Ravi Jandhyala[10], Gerd Moeller[11], Elena Levtchenko[12], and Zulf Murghal[13]

[1]Royal Manchester Children's Hospital, Manchester, UK; [2]Karolinska Institutet, Stockholm, Sweden; [3]APHP, Bicêtre Paris Sud Hospital, Le Kremlin Bicêtre, France; [4]University of Helsinki, Helsinki, Finland; [5]Lillebaelt hospital, Kolding, and University of Southern Denmark, Odense, Denmark; [6]Hospital Universitario Materno-Infantil Vall d'Hebron, Barcelona, Spain; [7]Center for Chronic Sick Children, Pediatric Endocrinology, Charité, University Medicine Berlin, Germany; [8]University of Florence, Florence, Italy; [9]University of Groningen, Groningen, The Netherlands; [10]Consultant KKI, Medialis Ltd, Banbury, UK; [11]Kyowa Kirin International, Galashiels, UK; [12]Katholieke Universiteit Leuven, Leuven, Belgium; [13]Royal Manchester Children's Hospital, Manchester, UK

OBJECTIVES

A European, multicentre, prospective, non-interventional observational registry has been launched to collect natural history data and characterise the treatment, disease progression and long-term outcomes in children and adults with X-Linked Hypophosphatemia (XLH).

INTRODUCTION

XLH is a rare, inherited disease, a disorder of renal phosphate wasting caused by high circulating levels of fibroblast growth factor 23 (FGF23) that impairs normal phosphate reabsorption in the kidney and production of the active form of vitamin D[1].1 There is currently no international registry that collects large-scale data on XLH disease progression and treatment outcomes.

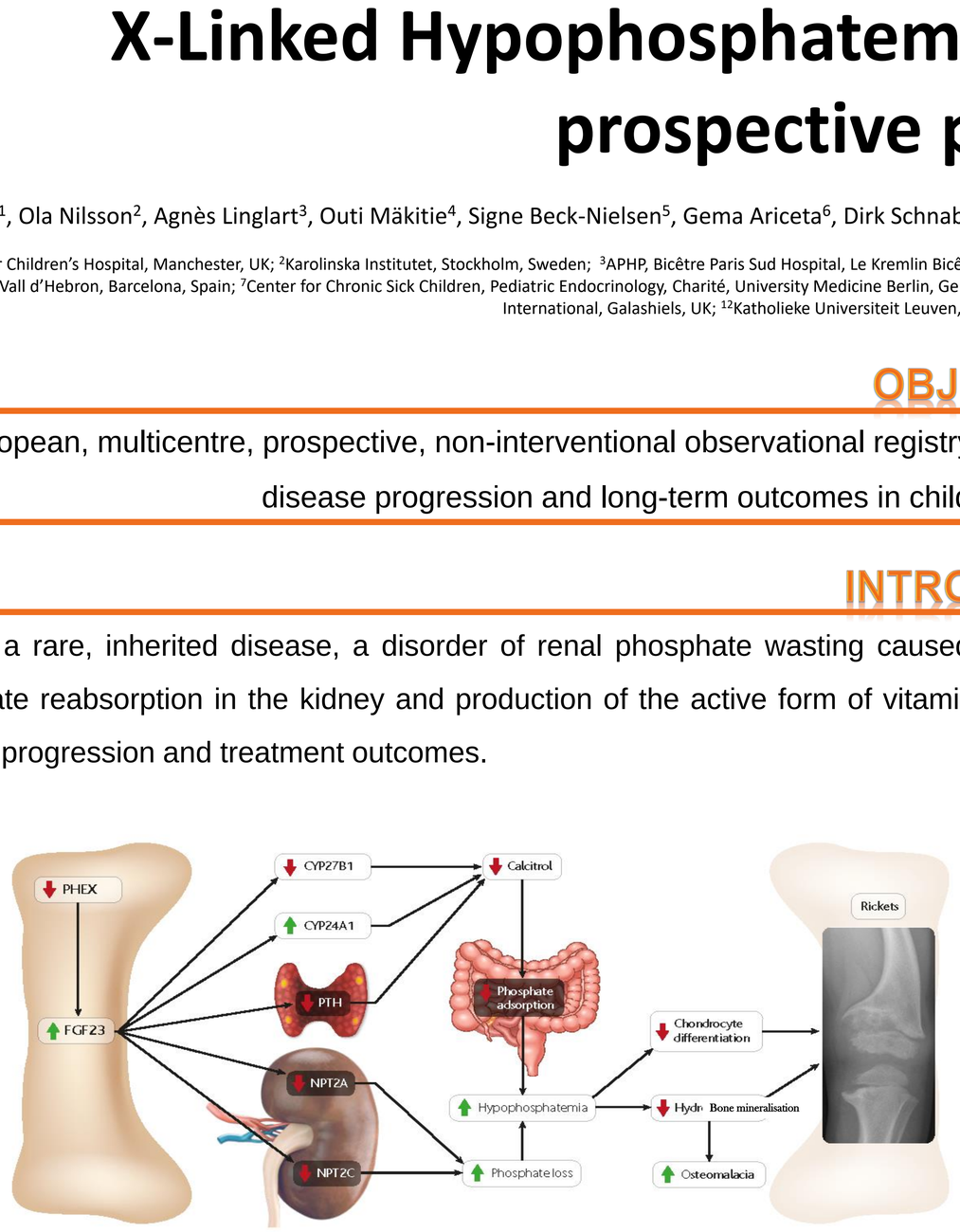


Figure 1. FGF23-vitamin D-phosphate axis. PHEX (Phosphate Regulating Endopeptidase Homolog, X-Linked), CYP24A1 (Cytochrome P450 family 24 subfamily A member 1), CYP27B2 (Cytochrome P450 family 27 subfamily B member 2), PTH (Parathyroid hormone), NPT2C and NPT2A (renal sodium-dependent phosphate co-transporter genes).

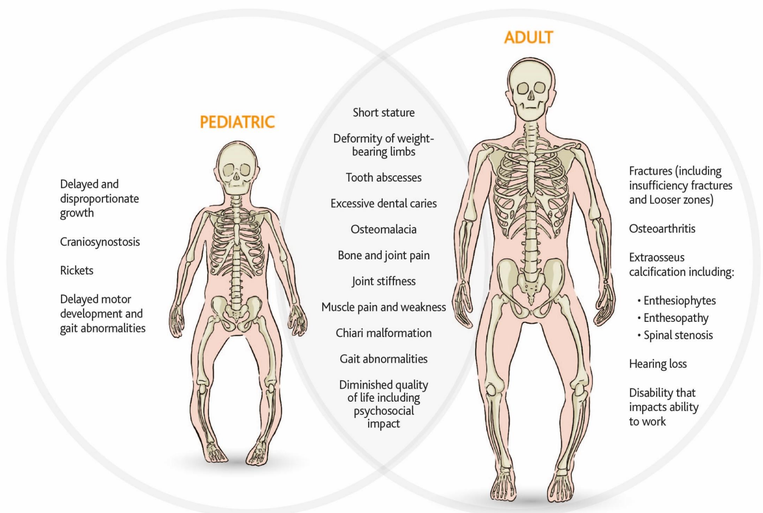


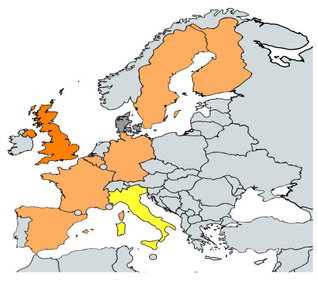
Figure 2. The signs, symptoms, sequelae, and long-term consequences of XLH in pediatric (left) and adult (right) patients.

METHODS

Design and implementation of the registry (NCT03193476)[2] was informed by recommendations from a recent European Medicines Agency, Patient Registries Workshop, (EMA/69716/2017)[3] and approved by a steering committee of European experts. The Registry is planned to run for at least 10 years, with an aim to recruit 1200 patients in total; patients with confirmed XLH will be included in the registry under informed consent. As a non-interventional study, all data entered will be from routine practice at the participating sites, measured at baseline and then prospectively at regular intervals; data entry is via an online data capture tool (Castor EDC, Netherlands). The registry will collect demographic variables, age and symptoms at diagnosis and family history, as well as quantitative and qualitative disease markers including: rickets, bone deformities, growth, oral health, muscular function, quality of life, phosphate wasting, alkaline phosphatase; and complications including nephrocalcinosis, hyperparathyroidism, hearing loss and neurological features. No data nor investigations are mandated by the protocol.

RESULTS

The XLH registry has currently recruited 50 patients from 50 sites across the UK, France, Denmark, Germany, Sweden and Italy. National regulatory approval is pending in The Netherlands, Belgium and Norway, and a total of 62 sites are expected to be live by December 2018.



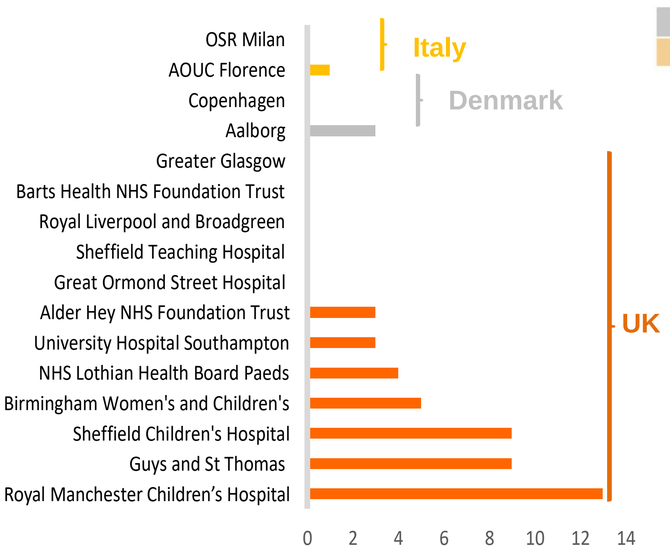


Figure 4. XLH Patient Recruitment per Centre

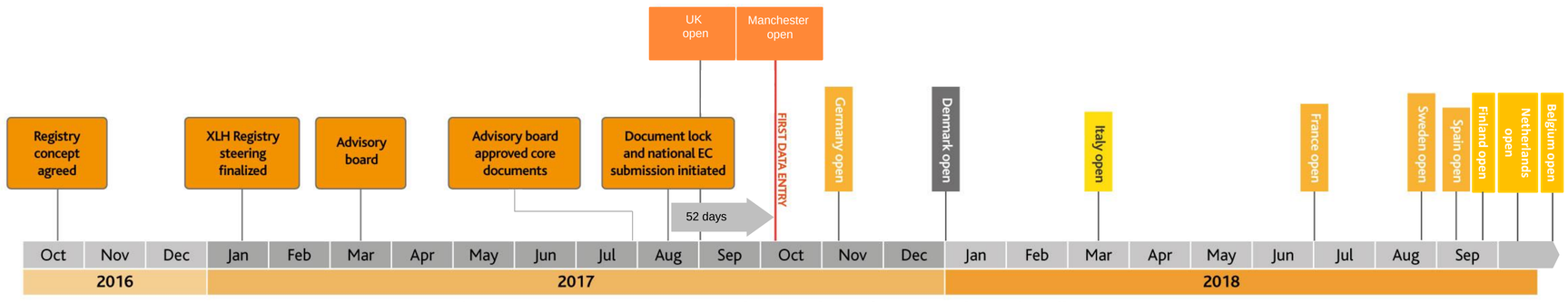


Figure 3. XLH Registry Design and Implementation Timeline

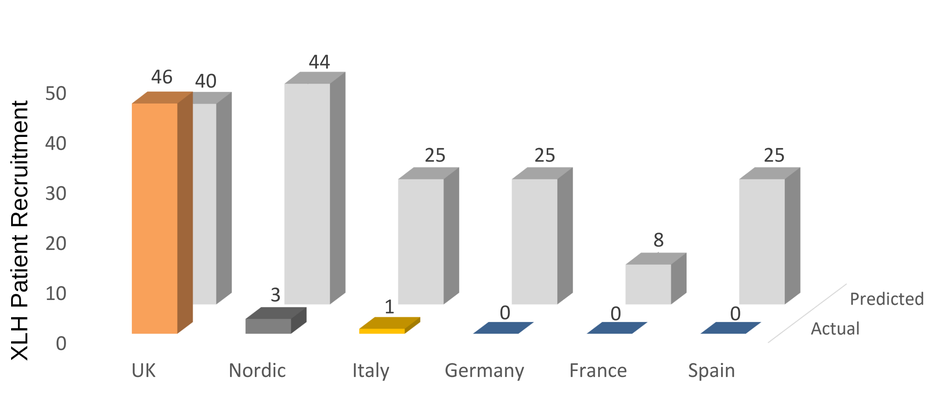
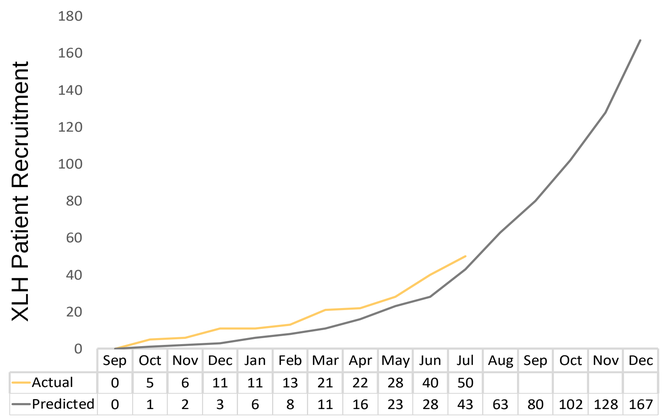


Figure 5. XLH Patient Recruitment per Country by August 2018



	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Actual	0	5	6	11	11	13	21	22	28	40	50					
Predicted	0	1	2	3	6	8	11	16	23	28	43	63	80	102	128	167

Figure 6. XLH Registry Patient Recruitment

CONCLUSIONS

✓ The XLH Registry will facilitate the generation of epidemiological data that will enhance and improve understanding of the natural history and disease burden of XLH, as well as long-term outcomes in patients with XLH

✓The XLH registry will help describe the effectiveness and safety of treatments used to manage the symptoms and signs of XLH

✓The XLH registry will support development of future XLH treatment guidelines and inform best practice

References:
1 Ruppe MD. X-Linked Hypophosphatemia. (Adam M, Ardinger H, Pagon R, eds.). University of Washington, Seattle; 2017
2 Registry for Patients With X-Linked Hypophosphatemia-ClinicalTrials.Gov, June, 2017. https://clinicaltrials.gov/ct2/show/NCT03193476
3 European Medicines Agency. Patient Registries Workshop, October, 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/02/WC500221618.pdf

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