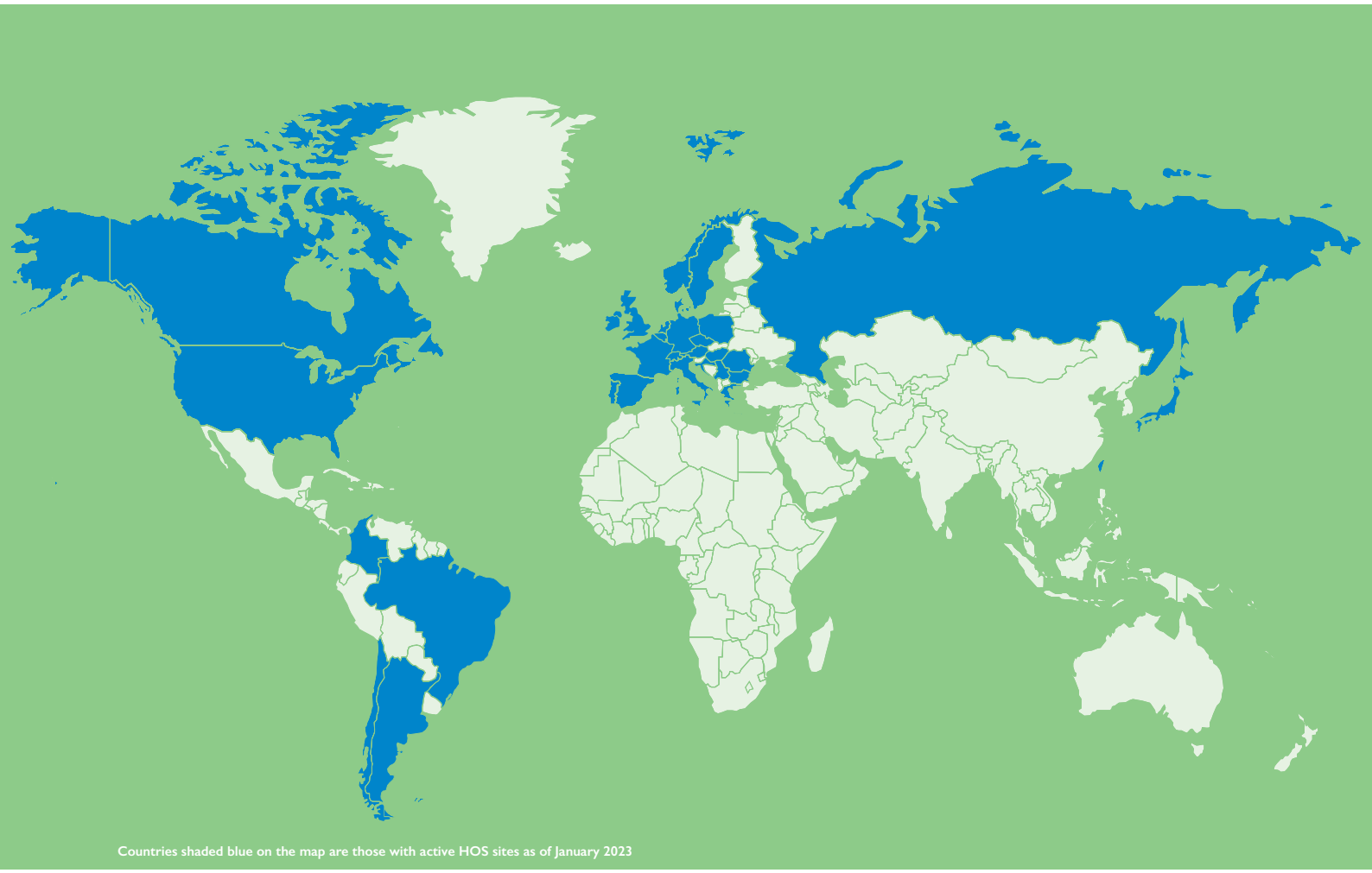
Hunter Outcome Survey



Countries shaded blue on the map are those with active HOS sites as of January 2023

2023 annual update for patient organizations

To provide information on registry developments and data in the registry as of 23 January 2023

hunter outcome survey

This report has been prepared by Takeda on behalf of the HOS Steering Committee

Date of preparation: August 2023
Item code: VV-MEDMAT-88039

hos
hunter outcome survey

Welcome

I am delighted to welcome you to the 2023 update on the Hunter Outcome Survey (HOS). HOS is a large disease registry, sponsored by Takeda, that was set up in 2005 to collect detailed information on patients with mucopolysaccharidosis II (MPS II; Hunter syndrome). HOS has facilitated the collection of data on the signs, symptoms and progression of MPS II and the experiences of patients, whether untreated or treated with idursulfase.

HOS has been running for over 17 years, and the difficult decision has now been made to close the registry. The original objectives of the project have been met and many questions regarding the long-term safety and effectiveness of treatment have been answered. HOS has made many important contributions to the understanding of the natural history of MPS II, with more than 20 manuscripts published in peer-reviewed journals and more than 60 oral presentations and posters presented at scientific meetings.

On behalf of the HOS Steering Committee and the team at Takeda, I would like to thank all patients and their caregivers who have provided such valuable contributions to HOS over the years. There are further publications planned using data from HOS, and a final report will be developed. For this reason, it is vital that we continue to collect data to ensure that they are as complete as possible. Takeda would like to reassure you that the company's commitment to the MPS II community will continue.

This report includes an update on patients enrolled in HOS as of January 2023. We hope that it will help patients and caregivers who are involved with or interested in MPS II to improve their understanding of the role of HOS and what has been learned to date.

BOB STEVENS
Patient organization representative on the HOS Steering Committee

This report is for information purposes only. It should not be used for diagnosing or treating a health problem or disease, and it should not be used instead of a consultation with a healthcare professional. Please consult your healthcare professional for further advice.

Any questions?

If so, please get in touch with one of the following contacts:

BOB STEVENS (Chief Executive of the MPS Society, UK)
Email: b.stevens@mpssociety.org.uk
NEIL YADAV (Clinical Project Manager, Takeda)
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Email: beth.daro-kaftan@takeda.com

What was HOS and what did it help us to investigate?

Who was eligible to take part in HOS?

- All patients (adults and children) with a diagnosis of MPS II who:
  - were untreated
  - were receiving or had previously received treatment with the enzyme replacement therapy (ERT) idursulfase
  - had previously received at least one haematopoietic stem cell transplant or bone marrow transplant.
- HOS also collected information on patients who were no longer alive.
- Patients were not eligible to participate in HOS if they were receiving an ERT other than idursulfase or were already taking part in a clinical trial.
- Patients continued to be cared for and treated by their own healthcare professionals.

What information was collected?

- During a patient's regular visit to their physician, information was collected and entered into HOS. This information included:

basic information (e.g. height, weight and age)

medical history (e.g. age at which the first symptoms were experienced, age at diagnosis, surgeries and other medical events)

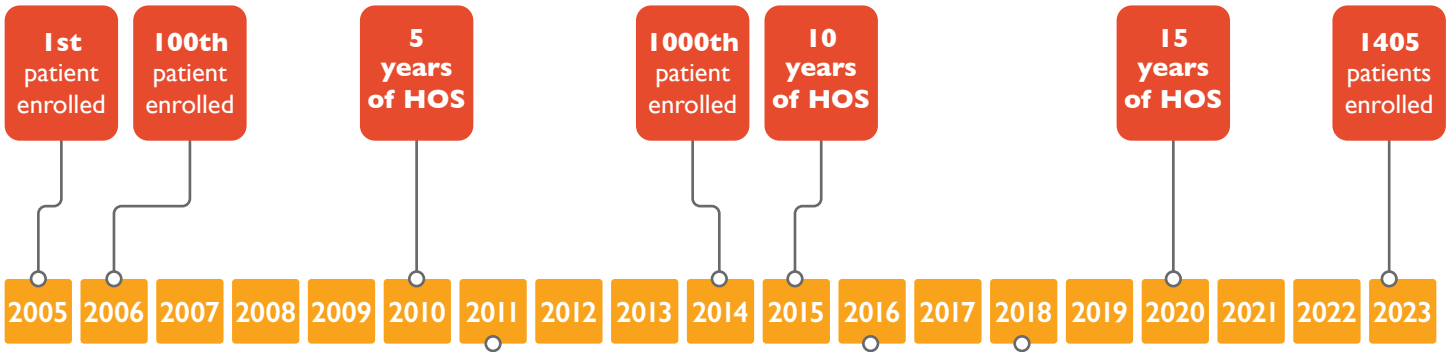
medical tests (e.g. blood and urine tests, genetic tests, and heart and breathing function tests)

any treatment(s) received and details of any side effects experienced.

HOS has made important contributions to our understanding of MPS II and its management

Some findings from HOS are communicated in publications. The main milestones for HOS, including the publication of key manuscripts using HOS data, are summarized in the image below.

A full list of published findings from HOS is provided in the 'HOS publications' section on pages 10–12.



Key manuscripts

10th HOS manuscript published

2008 First published report from HOS

2010 Data on surgical history of patients with MPS II

2011 Data on idursulfase treatment in patients under 6 years of age

15th HOS manuscript published

2017 Review of findings from the first 10 years of HOS

2017 Data on survival of untreated and idursulfase-treated patients

20th HOS manuscript published

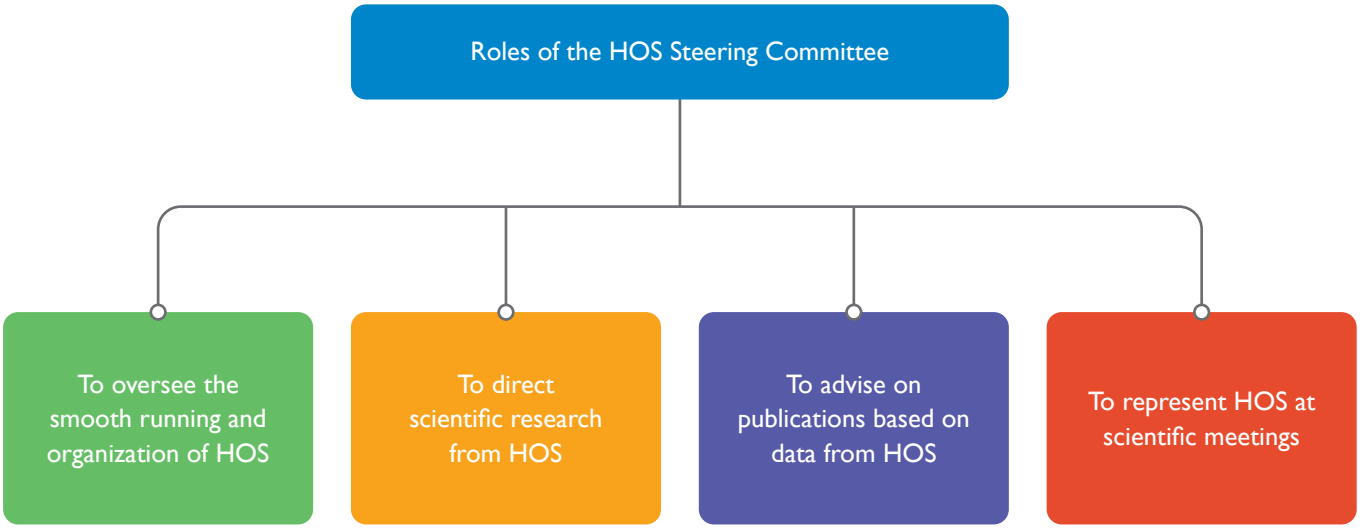
2021 Statistical modelling of the long-term effects of idursulfase

2021 Findings on the impact of the COVID-19 pandemic on patients with lysosomal storage diseases in HOS and other registries

hos hunter outcome survey

The HOS Steering Committee: who are they and what do they do?

Members of the HOS Steering Committee typically meet twice a year, helping to optimize HOS-related activities.



The HOS Steering Committee currently includes:

Twelve MPS II experts from around the world

- **Joseph Muenzer (Chair)**, Chapel Hill, NC, USA
- **Hernan Amartino**, Buenos Aires, Argentina
- **Barbara Burton**, Chicago, IL, USA
- **Roberto Giugliani**, Porto Alegre, Brazil
- **Paul Harmatz**, Oakland, CA, USA
- **Christoph Kampmann**, Mainz, Germany
- **Shuan-Pei Lin**, Taipei, Taiwan
- **Bianca Link**, Zurich, Switzerland
- **David Molter**, St Louis, MO, USA
- **Julian Raiman**, Birmingham, UK
- **Maurizio Scarpa**, Udine, Italy
- **Anna Tylki-Szymańska**, Warsaw, Poland

Four Takeda representatives

- **Siddharth Jain**, Global Medical Lead, MPS II and HOS Medical Monitor
- **Jaco Botha**, HOS Biostatistician Lead
- **Beth Daro-Kaftan**, HOS Publications Lead
- **Neil Yadav**, HOS Registry Lead

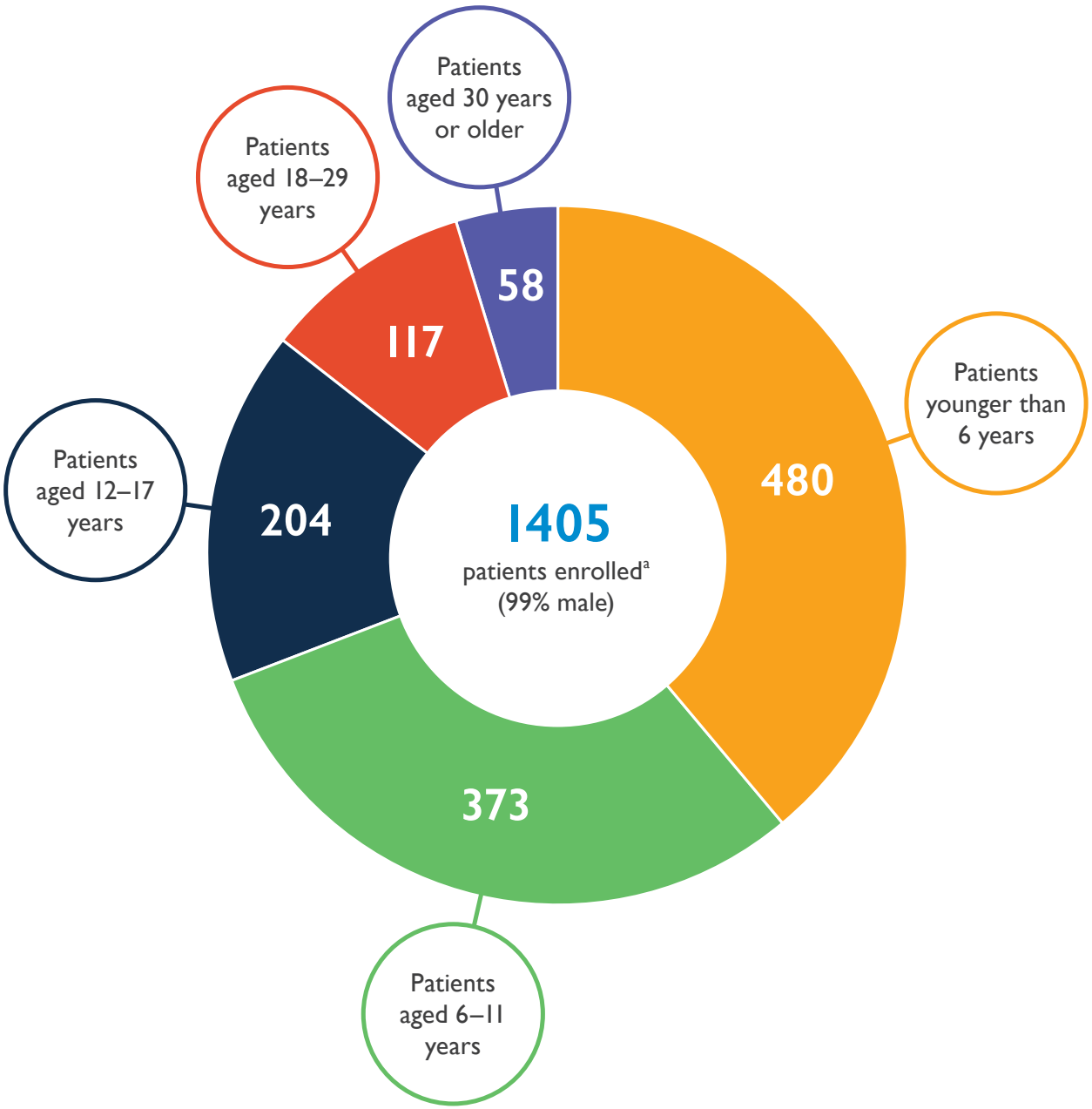
One patient organization representative

- **Bob Stevens**, MPS Society, UK

What were the characteristics of patients enrolled in HOS?

Update as of January 2023

Number of patients in HOS



[a]HOS included 1235 patients who were alive when they joined HOS and 170 who had their information entered into HOS after they had died, bringing the total to 1405 patients. The age groups shown in the image here are ages at joining HOS for those patients who were alive when they joined.

hos hunter outcome survey

Patients enrolled in HOS came from countries across the world

Total number of countries: 34

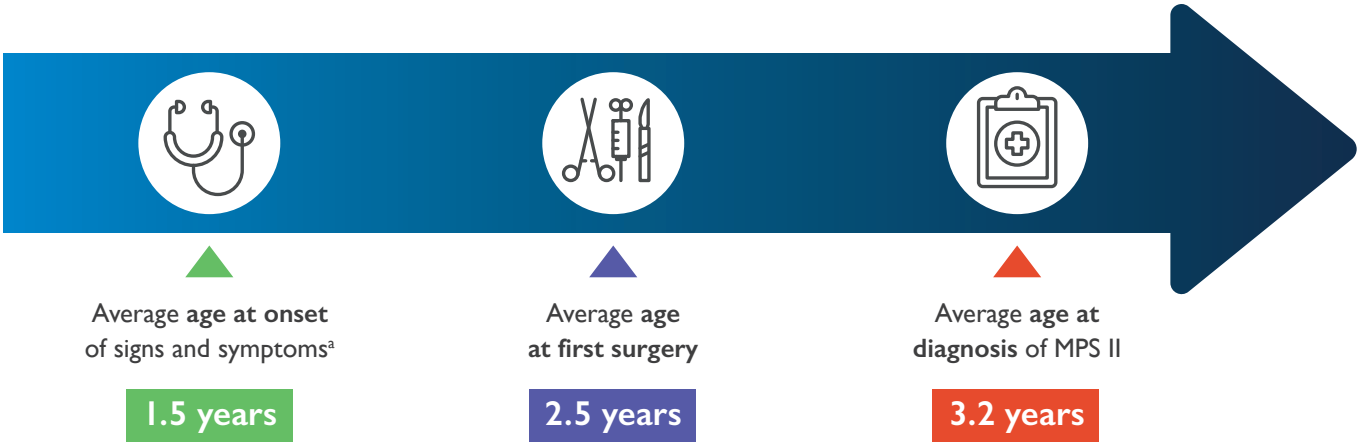
Total number of study sites: 157

Total number of patients: 1405

Country	Number of study sites	Number of patients
USA	41	326
UK	6	183
Brazil	8	160
France	4	97
Germany	5	80
Taiwan	12	64
Italy	13	62
Spain	19	59
Argentina	3	51
Poland	1	46
Canada	4	33
Russia	3	30
Romania	1	24
Austria	3	20
Sweden	4	19
Czech Republic	1	18
Netherlands	1	17

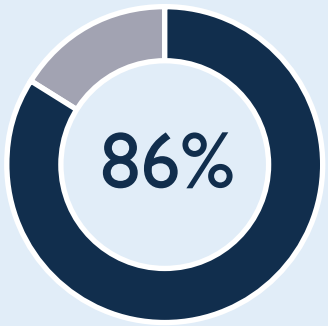
Country	Number of study sites	Number of patients
Colombia	1	12
Venezuela	1	11
Ireland	1	10
Portugal	3	10
Hungary	1	9
Belgium	5	8
Denmark	1	8
Norway	3	7
Chile	1	7
Greece	2	6
Mexico	1	5
Serbia	1	5
Croatia	2	4
Switzerland	2	4
Bulgaria	1	4
Japan	1	4
Peru	1	2
Total	157	1405

Age at symptom onset, first surgery and diagnosis for patients in HOS



Averages presented are median values (the median is the middle number in a list of numbers that are arranged by value). These data are for patients who were alive when they joined HOS.
[a]This refers to signs and symptoms likely attributable to MPS II.

Surgeries among patients in HOS

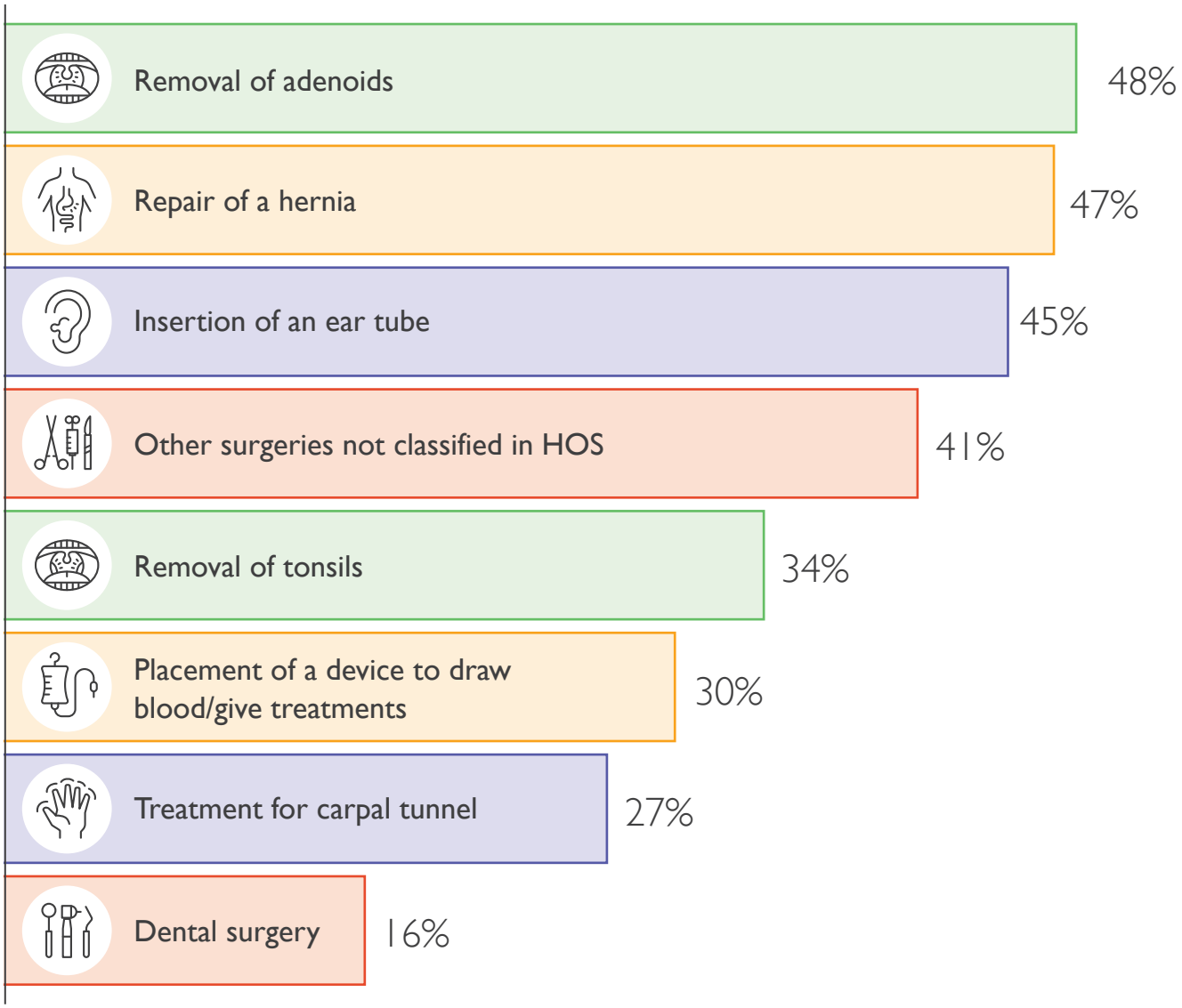


More than **8** out of **10** patients had at least **one** surgical procedure.

Among patients who had at least one surgical procedure, the average number of surgeries per patient was **5**.

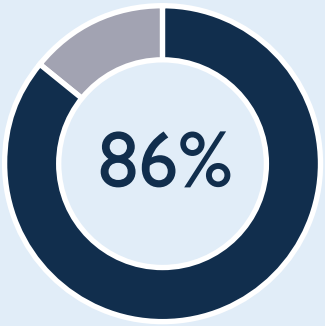
Averages presented are median values (the median is the middle number in a list of numbers that are arranged by value). These data are for patients who were alive when they joined HOS.

Proportion of patients in HOS who had undergone different surgeries



Surgeries performed in more than 10% of patients in HOS are shown.
These data are for patients who were alive when they joined HOS.

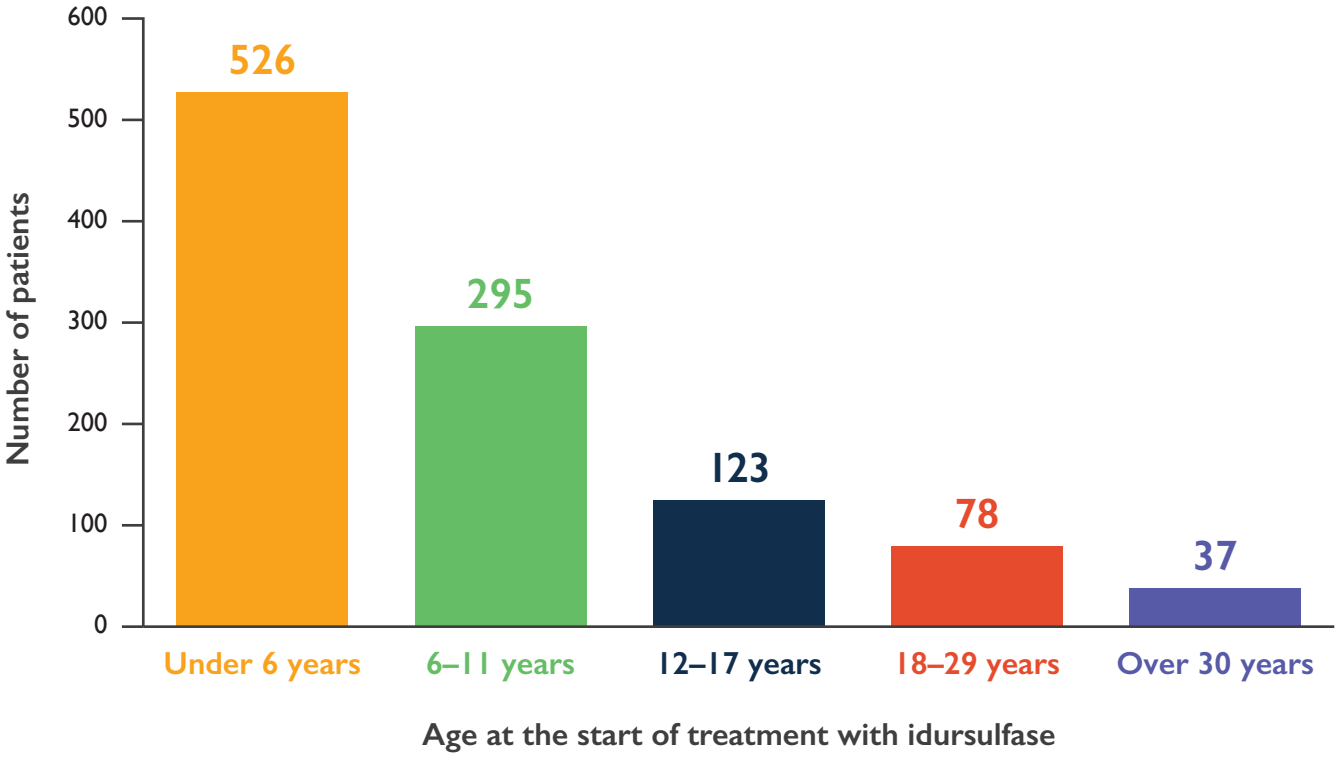
Patients in HOS who had received treatment with idursulfase



More than **8** out of **10** patients were treated with idursulfase at any time.

These data are for patients who were alive when they joined HOS.

Numbers of patients of different ages in HOS who had been treated with idursulfase



These data are for patients who were alive when they joined HOS.

HOS publications

To help raise awareness of MPS II and keep the MPS II community up to date, it is important for the findings from HOS to be shared publicly. This can be achieved through the publication of articles in scientific journals and by presentations at conferences. Crucially, HOS publications can be used to inform future research and help clinicians provide the best possible care for their patients.

The publication of findings from HOS remains an important priority despite the decision to close the registry. A poster reporting HOS data was presented at a key scientific conference in 2022. No new HOS manuscripts were published in 2022, but several are either being worked on or are planned for the future.

HOS poster presentations

- **One** poster using information from HOS was presented at the 2022 Society for the Study of Inborn Errors of Metabolism Annual Symposium.
  - This poster focused on the unmet needs of adult patients living with MPS II.

HOS manuscripts

A list of all of the published HOS manuscripts is shown below.

In total, 23 articles containing information from HOS have been published in scientific journals (up to January 2023).

Journal article (main topic in **bold**)	Link to journal website
HOS overview	
Muenzer J and co-authors. **Ten years of the Hunter Outcome Survey (HOS)**: insights, achievements, and lessons learned from a global patient registry. *Orphanet J Rare Dis* 2017;12:82.	
del Toro-Riera M. **Follow-up of patients** with Hunter syndrome: the Hunter Outcome Survey (HOS) registry. *Rev Neurol* 2007;44 (Suppl 1):S13–17 [written in Spanish].	

Journal article (main topic in **bold**)	Link to journal website
COVID-19 pandemic	
Elstein D and co-authors. **Impact of the COVID-19 pandemic** on the standard of care for patients with lysosomal storage diseases: a survey of healthcare professionals in the Fabry, Gaucher, and Hunter Outcome Survey registries. *Mol Genet Metab Rep* 2021;28:100788.	
Patient characteristics	
Lin H-Y and co-authors. **Clinical characteristics and surgical history of Taiwanese patients** with mucopolysaccharidosis type II: data from the Hunter Outcome Survey (HOS). *Orphanet J Rare Dis* 2018;13:89.	
Ficicioglu C and co-authors. **Intrafamilial variability in the clinical manifestations** of mucopolysaccharidosis type II: data from the Hunter Outcome Survey (HOS). *Am J Med Genet A* 2018;176:301–10.	
Bodamer O and co-authors. **Birth weight** in patients with mucopolysaccharidosis type II: data from the Hunter Outcome Survey (HOS). *Mol Genet Metab Rep* 2017;11:62–4.	
Keilmann A and co-authors. **Hearing loss** in patients with mucopolysaccharidosis II: data from HOS – the Hunter Outcome Survey. *J Inherit Metab Dis* 2012;35:343–53.	
Kampmann C and co-authors. Prevalence and characterization of **cardiac involvement** in Hunter syndrome. *J Pediatr* 2011;159:327–31.e2.	
Link B and co-authors. **Orthopedic manifestations** in patients with mucopolysaccharidosis type II (Hunter syndrome) enrolled in the Hunter Outcome Survey. *Orthop Rev (Pavia)* 2010;2:e16.	
del Toro-Riera M. **World-wide experience** in the treatment of mucopolysaccharidosis type II: the Hunter Outcome Survey (HOS) registry. *Rev Neurol* 2008;47 (Suppl 2):S3–7 [written in Spanish].	
Wraith JE and co-authors. **Initial report** from the Hunter Outcome Survey. *Genet Med* 2008;10:508–16.	
Diagnosis	
Cohn GM and co-authors. Development of a **mnemonic screening tool** for identifying subjects with Hunter syndrome. *Eur J Pediatr* 2013;172:965–70.	
Mendelsohn NJ and co-authors. Importance of **surgical history** in diagnosing mucopolysaccharidosis type II (Hunter syndrome): data from the Hunter Outcome Survey. *Genet Med* 2010;12:816–22.	

Journal article (main topic in **bold**)	Link to journal website
Disease progression and outcomes	
Muenzer J and co-authors. Evaluation of the **long-term treatment effects** of intravenous idursulfase in patients with mucopolysaccharidosis (MPS II) using statistical modeling: data from the Hunter Outcome Survey (HOS). *Orphanet J Rare Dis* 2021;16:456.	
Burton BK and co-authors. **Survival** in idursulfase-treated and untreated patients with mucopolysaccharidosis type II: data from the Hunter Outcome Survey (HOS). *J Inherit Metab Dis* 2017;40:867–74.	
Muenzer J and co-authors. **Clinical outcomes** in idursulfase-treated patients with mucopolysaccharidosis type II: 3-year data from the Hunter Outcome Survey (HOS). *Orphanet J Rare Dis* 2017;12:161.	
Parini R and co-authors. **The natural history of growth** in patients with Hunter syndrome: data from the Hunter Outcome Survey (HOS). *Mol Genet Metab* 2016;117:438–46.	
Jones SA and co-authors. The effect of idursulfase on **growth** in patients with Hunter syndrome: data from the Hunter Outcome Survey (HOS). *Mol Genet Metab* 2013;109:41–8.	
Burton BK and Whiteman DAH. Incidence and timing of **infusion-related reactions** in patients with mucopolysaccharidosis type II (Hunter syndrome) on idursulfase therapy in the real-world setting: a perspective from the Hunter Outcome Survey (HOS). *Mol Genet Metab* 2011;103:113–20.	
Muenzer J and co-authors. Idursulfase **treatment** of Hunter syndrome **in children younger than 6 years**: results from the Hunter Outcome Survey. *Genet Med* 2011;13:102–9.	
Alcalde-Martín C and co-authors. First experience of enzyme replacement therapy with idursulfase in **Spanish patients with Hunter syndrome under 5 years of age**: case observations from the Hunter Outcome Survey (HOS). *Eur J Med Genet* 2010;53:371–7.	
Burton BK and co-authors. **Home treatment** with intravenous enzyme replacement therapy with idursulfase for mucopolysaccharidosis type II — data from the Hunter Outcome Survey. *Mol Genet Metab* 2010;101:123–9.	
Jones SA and co-authors. **Mortality and cause of death** in mucopolysaccharidosis type II — a historical review based on data from the Hunter Outcome Survey (HOS). *J Inherit Metab Dis* 2009;32:534–43.	

Thank you for reading this annual HOS update.
If you have any questions, please get in touch with one of the contacts listed on page 1.