Patient reported outcomes in MPS IVA patients receiving enzyme replacement therapy:

The patient reported experience after the first two years on an English managed access agreement

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Background

- Morquio A syndrome (MPS IVA) is an ultra-rare, inherited, multi-systemic disease which, if untreated, results in impaired functioning, mobility, and quality of life (QoL), and early death[1]
- Enzyme replacement therapy (ERT) with elosulfase alfa is the only approved treatment
- Since December 2015, individuals with MPS IVA in England have had access to elosulfase alfa via a managed access agreement (MAA)[2]
- Under the MAA, patients are monitored clinically and via patient reported outcomes (PROs) using standard tools: MPS HAQ, EQ-5D-5L, Adolescent Paediatric Pain Tool, Brief Pain Inventory and the Beck Depression Inventory
- While collecting the PROs for the MAA, MPS Commercial has undertaken their own research to capture changes reported by patients in their own words that may not be captured using standard tools
- Reported changes for those patients completing the first two years of the five year programme are reported herein

Methods

- Testimonies were collected during the patient's MAA PRO assessments, either over the telephone or through e-mail communication
- ERT naïve patients were asked at 4, 8 and 12 months on treatment under the MAA if they had noticed any changes since starting treatment
  - At 24 months, ERT naïve patients were asked if they had noticed any changes in the last year
- Patients who previously received elosulfase alfa as part of a clinical trial were asked at 12 and 24 months after joining the MAA if they had noticed any changes in the last year
- Changes were reported by either the patient or their parent/carer (in those aged under 18 years)
- Informed consent was sought to collect and share testimony data
- The changes reported by patients were grouped under the following headings for analysis:

Energy · Walking and movement · Sleep/tiredness · Pain · Thinking/learning · Appearance · General health · Specific health changes · No change

Results

- Of the 56 patients who had completed at least 4 months on the MAA, 42 consented to their testimonies being shared; a total of 99 testimonies were reported
- Patients were aged between 1–58 years when they joined the MAA; mean age was 29.5 years
- Twenty-two patients were elosulfase alfa naïve on entering the MAA; 20 patients had previously received elosulfase alfa as part of a clinical trial (Table 1)
- Not all patients joined the MAA at the same time or provided a testimony at each applicable time point; the number of patients at each of the testimony collection time points reflects this

Table 1. Number of patients providing testimonies

	Naïve patients	Elosulfase alfa trial patients
Children (under 18 years)	13	11
Adults (18 years or over)	9	9

After 4 months on the MAA

- After 4 months on treatment on the MAA, 17 testimonies were collected from naïve patients reporting 49 changes
- The most commonly reported changes affected the patient's energy levels (10/49, 20%), walking and movement (9/49, 18%) and pain (8/49, 16%) (Table 2)

Table 2. Reported changes in naïve patients after 4 months on the MAA

% of reported changes N=49	Specific changes reported
Energy (20%)	Increased energy (n=6), more active (n=2), everyday activities easier (n=1), ability to do more in a day (n=1)
Walking and movement (18%)	Walking easier/more (n=2), easier movement (n=2), less stiff (n=1), more toned (n=1), arm/hands/wrists stronger (n=1), expected more from walking (n=1), resilience to cope with hip (n=1)
Sleep/tiredness (10%)	Less tired (n=3), better sleep (n=1), wakes up earlier (n=1)
Pain (16%)	Less pain (n=4), using less pain medication (n=2), not waking in the night with pain (n=1), noticing pain when infusion is due (n=1)
Thinking/ learning (10%)	More clarity of thought (n=1), better concentration (n=1), increased vocabulary (n=1), wanting to learn (n=1), better hand-eye coordination (n=1)
Appearance (4%)	Better skin complexion (n=2)
General health (10%)	Growth (n=2), not as ill (n=1), better appetite (n=1), happier in themselves (n=1)
Specific health changes (4%)	Fewer headaches (n=1), breathing better (n=1)
No change (6%)	No change/nothing to report (n=3)

After 8 months on the MAA

- At 8 months, 18 testimonies were collected from naïve patients with 79 reported changes
- The most commonly reported changes affected the patient's general health (22/79, 28%), walking and movement (17/79, 22%) and energy levels (13/79, 16%) (Table 3)

Table 3. Reported changes in naïve patients after 8 months on the MAA

% of reported changes N=79	Specific changes reported
Energy (16%)	Increased energy (n=7), ability to do more in a day (n=4), more active (n=2)
Walking and movement (22%)	Walking easier/more (n=5), feeling stronger (n=3), less stiff (n=1), arm/hands/wrists stronger (n=1), more toned (n=1), able to carry bags (n=1), no deterioration in physical ability (n=1), able to transfer from/to wheelchair better (n=1), able to move more (n=1), able to bear weight on feet for longer (n=1), less movement when infusion is due (n=1)
Sleep/tiredness (8%)	Less tired (n=3), feeling tired (n=2), drained the day after infusion (n=1)
Pain (11%)	Less pain (n=5), using less pain medication (n=1), not waking in the night with pain (n=1), noticing pain when infusion is due (n=1), more comfortable (n=1)
Thinking/learning (3%)	More clarity of thought (n=1), more engaged (n=1)
Appearance (4%)	Better skin complexion (n=2), slight dryness of skin (n=1)
General health (28%)	Happier in themselves (n=4), growth (n=3), not as ill (n=2), better appetite (n=2), weight gain (n=2), more confidence (n=2), improvement in quality of life (n=2), improved mood (n=2), ability to lose weight (n=1), funny dreams (n=1), stable/generally well (n=1)
Specific health changes (8%)	Breathing better (n=2), lungs clearer (n=1), feeling pressure on chest day before infusion (n=1), no recent chest infections (n=1), worsened short term memory (n=1)
No change (1%)	No change/nothing to report (n=1)

After 12 months on the MAA

- At 12 months, 19 testimonies were collected from naïve patients with 95 reported changes
- The most commonly reported changes in naïve patients affected their general health (24/95, 25%), energy levels (19/95, 20%) and sleep/tiredness (16/95, 17%) (Table 4)
- An additional 20 testimonies were collected from patients previously receiving elosulfase alfa as part of a clinical trial with 53 reported changes
- The most commonly reported changes in this group affected their energy levels (11/53, 21%), general health (10/53, 19%) and specific health benefits and walking and movement (both 7/53, 13%) (Table 4)

Table 4. Reported changes in naïve patients and patients previously receiving elosulfase alfa as part of a clinical trial after 12 months on the MAA

Naïve patients		Elosulfase alfa trial patients	
% of reported changes N=95	Specific changes reported	% of reported changes N=53	Specific changes reported
Energy (20%)	Increased energy (n=12), more stamina (n=3), everyday activities easier (n=1), ability to do more in a day (n=1), more active (n=1), physically active (n=1)	Energy (21%)	Increased energy (n=4), more stamina (n=2), no deterioration in energy levels (n=2), no deterioration in stamina (n=1), able to do more in the day (n=1), more active (n=1)
Walking and movement (14%)	Walking easier/more (n=5), easier movement (n=2), hands/wrists stronger (n=1), can manage steps (n=1), more toned (n=1), able to transfer from/to wheelchair better (n=1), able to stand longer without legs trembling (n=1), fine motor skills – no change, builds lego (n=1)	Walking and movement (13%)	Walking easier/more (n=3), no deterioration in physical ability/mobility (n=2), movement a lot better (n=1), feeling stronger (n=1), more toned (n=1)
Sleep/tiredness (17%)	Less tired (n=9), better sleep (n=4), felt better upon waking (n=3)	Sleep/tiredness (8%)	Less tired (n=2), better sleep (n=2)
Pain (6%)	Less pain (n=4), no pain (n=1), increased pain (n=1)	Pain (6%)	No pain (n=1), not waking in night with pain (n=1), back hurting more (n=1)
Thinking/learning (6%)	More engaged (n=3), more clarity of thought (n=1), better concentration (n=1), better handwriting (n=1)	Thinking/learning (9%)	More clarity of thought (n=1), better concentration (n=1), more engaged (n=1), behaviour improved (n=1), better handwriting (n=1)
Appearance (1%)	Better skin complexion (n=1)	Appearance (2%)	Skin better (n=1)
General health (25%)	Growth (n=4), weight gain (n=3), weight not changed much (n=1), happier in themselves (n=3), not as ill (n=2), better appetite (n=2), better social skills (n=2), missing less school (n=1), speech clearer and louder (n=1), ability to lose weight (n=1), more confidence (n=1), improved quality of life (n=1), more relaxed (n=1), improved mood (n=1)	General health (19%)	More independence (n=3), not as ill (n=2), happier in themselves (n=2), weight gain (n=1), ability to lose weight (n=1), generally well (n=1)
Specific health changes (9%)	Breathing better (n=3), lungs clearer (n=1), eyesight better (n=1), wears glasses now (n=1) better sense of smell (n=1), reduced number of ear infections (n=1), hearing improved, grommets fitted (n=1)	Specific health changes (13%)	Breathing better (n=2), less diarrhoea (n=1), lungs clearer (n=1), eyesight better (n=1), no recent chest infections (n=1), hearing slightly improved (n=1)
No change (1%)	No change/nothing to report (n=1)	No change (9%)	No change/nothing to report (n=5)

After 24 months on the MAA

- At 24 months, 6 testimonies were collected from naïve patients with 19 reported changes
- The most commonly reported changes in naïve patients affected their energy levels (4/19, 21%), walking and movement, sleep/tiredness, thinking/learning and general health (all 3/19, 16%) (Table 5)
- An additional 19 testimonies were collected from patients previously receiving elosulfase alfa as part of a clinical trial with 46 reported changes
- The most commonly reported changes in this group affected their general health and walking and movement (both 9/46, 20%) (Table 5)

Table 5. Reported changes in naïve patients and patients previously receiving elosulfase alfa as part of a clinical trial after 24 months on the MAA

Naïve patients		Elosulfase alfa trial patients	
% of reported changes N=19	Specific changes reported	% of reported changes N=46	Specific changes reported
Energy (21%)	Increased energy (n=2), more stamina (n=1), physically active (n=1)	Energy (13%)	Increased energy (n=3), more stamina (n=1), able to do more in the day (n=1), physically active (n=1)
Walking and movement (16%)	Walking easier/more (n=2), easier movement (n=1)	Walking and movement (20%)	Poor mobility (n=2), worsened posture (n=2), walking easier/more (n=1), continuing to get about [walking] (n=1), better grip (n=1), no deterioration in physical ability (n=1), posture is good (n=1)
Sleep/tiredness (16%)	Less tired (n=2), better sleep (n=1)	Sleep/tiredness (13%)	Feeling tired (n=2), less tired (n=2), better sleep (n=1), ability to manage tiredness better (n=1)
Pain (5%)	Increased pain (n=1)	Pain (7%)	Increased pain (n=2), little pain (n=1)
Thinking/learning (16%)	Better concentration (n=1), increased vocabulary (n=1), more engaged (n=1)	Thinking/learning (9%)	Better concentration (n=1), mental age improvement (n=1), started writing (n=1), following instructions (n=1)
Appearance	–	Appearance	–
General health (16%)	Better appetite (n=1), improved quality of life (n=1), more relaxed (n=1)	General health (20%)	Generally well (n=4), quality of life improved (n=3), growth (n=1), happier in themselves (n=1)
Specific health changes (11%)	Fewer headaches (n=1), eyesight better (n=1)	Specific health changes (9%)	Coughing/wheezing (asthma) worsened (n=1), corneal clouding improved (n=1), no recent chest infections (n=1), periods started again (n=1)
No change	–	No change (11%)	No change/nothing to report (n=2), no deterioration – on treatment since 2012 (n=1), stable since started treatment (n=1), remained stable, been on treatment 6 years (n=1)

– Not reported

Discussion

- During the first two years of the elosulfase alfa MAA, naïve patients most frequently reported changes in their energy levels and general health
- For patients who had previously received elosulfase alfa as part of a clinical trial, the most common areas of change reported during the MAA were walking and movement and general health
- Not all changes reported were positive, however, there were fewer negative reports in comparison
- The changes reported here reflect the overall patients' experience over a two year period on the MAA and therefore may not be attributable solely to treatment with elosulfase alfa
  - Some of the changes experienced in the younger patients may constitute a developmental effect e.g. improved handwriting or increased vocabulary
  - Other treatments or surgeries may have contributed to the changes reported
- It should be noted that under the terms of the MAA, elosulfase alfa treatment may be stopped if patients do not meet set criteria for continuation of treatment
  - Although the testimonies presented here are not part of the criteria to remain on the MAA, concerns over access to treatment may affect the information that patients are willing to share in their testimonies

Conclusions

- This study highlights a range of outcomes that are important to patients' lives that may not be collected via current standard PRO tools
- These findings may act as a guide to the selection of suitable tools or the development of disease specific measures for use in future studies

References

1 Hendriksz C *et al*. 2015. Am J Med Genet A;167A(1):11

2 NICE. Managed Access Agreement Elosulfase alfa for treating mucopolysaccharidosis type IVA. 16 December 2015. Available from: https://www.nice.org.uk/guidance/hst2/resources/managed-access-agreement-december-2015-2238935869 (Accessed 12 July 2018)

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