

## ARTICLE

# Home-based service for enzyme replacement therapy in lysosomal storage disorders: patient reported outcomes

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## Abstract

**Background:** Lysosomal storage diseases (LSDs) are a heterogeneous group of rare chronic genetic conditions. The standard-of-care treatment for LSDs is hospital-based infusion of enzyme replacement therapy (ERT), however, over time this can be stressful and inconvenient. The Italian TuTor program, established in 2011 by Sanofi Genzyme, is a professional nursing service providing home-based ERT to patients with LSDs.

**Objectives:** The current questionnaire-based study was conducted to investigate the level of patient satisfaction with the TuTor program and to shed light on disease perception.

**Methods:** Patients were enrolled in the TuTor program from 2011 onwards. The first 100 patients enrolled were interviewed at baseline with follow-up interviews conducted at 6, 12 and 18 months.

**Results:** Overall, 52 patients were female; 46 had Gaucher's disease, 46 had Fabry disease and 8 had mucopolysaccharidosis type 1. Patients took on average >2 hours to receive hospital-based ERT, plus time associated with the infusion; 2 out of 3 patients needed a caregiver to travel to the hospital. After receiving home-based ERT for 6 months, 37% of patients considered their quality of life 'greatly improved' (60% at 18 months). Overall, 99% to 100% of patients rated the home-based nursing service as 'positive' or 'very positive' and reported that they would recommend the service to other patients with their condition.

**Conclusions:** For patients with LSDs eligible for ERT, a disease-specific home-based nursing service increased their perception of quality of life over a hospital-based service and was advantageous in terms of their time and expenditure.

## Keywords

Lysosomal storage diseases, enzyme replacement therapy, home-based therapy, nursing service, patient-reported outcomes, patient satisfaction, person-centered healthcare, quality of life

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## Introduction

Lysosomal storage diseases (LSDs) are a heterogeneous group of rare genetic disorders characterized by the progressive accumulation of various substrates within the lysosomes [1]. While each one of these disorders is individually rare, together the overall incidence of LSDs

has been estimated at around 1 in 4,000 to 1 in 8,000 live births [1-4].

LSDs are subdivided by the type of enzyme involved and the substrate that accumulates [5]. The hallmark of Gaucher's disease, which is one of the best characterized LSD, is the accumulation of sphingolipids, specifically glycosylceramide, in the spleen, liver and bone [6,7].

Gaucher's disease, caused by mutations in the *GBA1* gene which leads to a decreased activity of the lysosomal enzyme, glucocerebrosidase, is inherited in an autosomal recessive manner and has an incidence in the general population of around 1 in 40,000 to 1 in 60,000 live births [8].

Another well characterized LSD is Fabry disease, an X-linked lysosomal storage disorder caused by a deficiency of the lysosomal enzyme,  $\alpha$ -galactosidase A, which results in the systemic accumulation of globotriaosylceramide and related glycosphingolipids within lysosomes [9]. Fabry disease has an estimated prevalence of 1 in 40,000 to 1 in 170,000 live births and can lead inexorably to progressive renal failure, heart failure and stroke later in life, with morbidity and reduced life expectancy related to the extent of end-organ damage [9].

Mucopolysaccharidosis type 1 (MPS-1) is an ultra-rare autosomal recessive disease with a very low incidence in the general population (1 in 100,000) [1,10]. MPS-1 is caused by a deficiency of alpha-L-iduronidase causing the accumulation of glycosaminoglycans within tissues, eventually leading to organ and tissue damage [10].

The standard-of-care treatment for LSDs, whenever available, is enzyme replacement therapy (ERT) [4,10,11]. ERT, in which the mutated lysosomal enzyme is replaced by a recombinant wild-type enzyme delivered intravenously, is approved worldwide for the treatment of Gaucher's disease, Fabry disease and MPS-1 [4], although agalsidase alfa (Replagal, Shire) still remains unapproved by the U.S. Food and Drug Administration for the treatment of Fabry disease and taliglucerase alfa (Uplyso, Pfizer) is not approved in Europe for the treatment of Gaucher's disease. While extensive clinical trials as well as real-world studies have confirmed the efficacy and safety of ERT, treatment with ERT for LSDs is life-long, with disease progression observed in cases of poor adherence or when infusions are regularly missed [4,11].

From the individual patient's perspective, there are a few downsides to ERT, particularly the need for regularly taking time out of work or school to receive therapy in hospital, or the requirement for patients to travel long distances to their nearest center for infusion, which can place a considerable burden on the patient and their caregivers [12]. The time spent in hospital to receive therapy can also negatively impact quality of life [11], as parents/guardians of children with LSDs have reported that ERT in hospital is disruptive for their own work, interferes with school and is generally stressful and inconvenient [5].

In 2011, Sanofi Genzyme established the TuTor program in Italy, a home-based professional nursing service that can be activated upon request by treating physicians. The TuTor program was established for the home-based delivery of ERT for the treatment of rare disorders including: imiglucerase (Cerezyme® [13]) for Gaucher's disease; agalsidase beta (Fabrazyme® [14]) for Fabry disease and laronidase (Aldurazyme® [15]) for MPS-1.

A questionnaire-based study was conducted to investigate the level of patient satisfaction with the TuTor service and to shed light on disease perception. Here we present data from patient satisfaction questionnaires of the first 100 patients enrolled in the TuTor program covering

the first 18 months of their experience of the home-based nursing service.

## Methods

The TuTor program is currently offering home-based ERT treatment to 138 patients in Italy and relies on 45 professional nurses. The first 100 patients enrolled sequentially in the TuTor program were included in this questionnaire-based study. Of these, 8 patients were enrolled in 2011, 12 patients in 2012, 30 patients in 2013, 26 patients in 2014 and 24 patients in 2015. All 100 patients were first interviewed by telephone (at baseline) and at the time of the first follow-up survey, at 6 months. Eighty-one patients also completed the second interview at 12 months and 65 patients were interviewed at 18 months. The decrease over time in the number of patients surveyed was simply due to the sequential time for enrolment and to the date of data extraction (in 2016), which resulted in a number of patients enrolled in 2014 and 2015 not being included at all time points in this analysis.

Dosage and frequency of ERT administration were in accordance with the European Medicines Agency labeling. All patients with Gaucher's disease received infusions of imiglucerase 30-60 U/Kg once every 2 weeks, depending on the severity of the disease and achievement of therapeutic goals [13]. All patients with Fabry disease were treated with agalsidase beta 1 mg/Kg once every two weeks [14]. All patients with MPS-1 were treated with laronidase 100 U/Kg once a week [15].

Patients participated in telephone interviews conducted by the TuTor call center (TuTor service assistance center). This center provides support for both nurses and patients regarding the schedule of appointments for ERT infusions and for any related queries that may arise. Patients were interviewed at baseline, prior to switching from hospital-based infusion therapy to the home-based service, with follow-up interviews subsequently conducted every 6 months.

At baseline, the needs, time spent and costs related to hospital visits for the administration of therapy were collected. This involved the assessment of whether a patient had taken leave from work in order to receive hospital-based infusion therapy, the average distance travelled and time taken to get to the hospital, the period of time spent waiting at the hospital prior to starting infusion therapy and afterwards during the observation period for the monitoring of any adverse events and time spent waiting to be discharged. Patients were also questioned on their means of transport and associated costs and whether they required the support of a caregiver in order to attend hospital infusions.

Follow-up surveys were conducted every 6 months and assessed patients' long-term perception of health with the TuTor service and the quality of service provided by the TuTor nurses and the TuTor call service personnel. Patients were also questioned on their acceptance of receiving infusion therapy at home, their overall level of satisfaction with the TuTor home-based nursing service and, most importantly, whether they would recommend this service to

other patients with the same condition.

## Compliance with Ethics Guidelines

Home infusion of all 3 ERTs is compliant with European and national regulations. Clinicians proposed the TuTor service to eligible patients who, in case of acceptance, provided their informed consent to participate in the survey. Patients might retire their consent at any time and still continue to be enrolled in the TuTor service.

## Results

### Patient characteristics

The first 100 patients enrolled in the TuTor program were included in this questionnaire-based study. Of these, 52 were female and 48 were male. Patients' age ranged from 5 to 80 years, with an age range of 7 to 80 years for patients with Gaucher's disease (n=46), 14 to 80 years for Fabry disease (n=46) and 5 to 44 years for MPS-1 (n=8). Geographically, the patients were distributed across Italy with the majority (58%) residing in the South and the Islands, 24% from the North West, 16% from the Center and 2% from the North East.

### Hospital-based enzyme replacement therapy

At baseline, when all 100 patients were interviewed about their hospital-based ERT prior to entering the home-based service, 27% of patients reported 'always' having to take leave from work to go to hospital to receive ERT, with a further 8% reporting 'sometimes' (n=6) or 'often' (n=2) having to do so.

Fifty-seven percent of patients reported they 'always' had a family member or friend with them when attending hospital to receive ERT, with a further 12% reporting that a companion was 'sometimes' (n=7) or 'often' (n=5) required. Among the 69 patients who reported ever having a family member or friend attend hospital visits with them, 23% of those family members or friends were also required to take leave from work each time, with a further 10% 'sometimes' (n=6) or 'often' (n=4) having to take leave from work.

Approximately half of the patients (47%) had to travel between 11 and 30 km to receive ERT, with 1 in 4 patients (24%) having to travel further than 30 km. The average travel time was approximately 44 minutes, with 47% of patients having to travel for >30 minutes. However, these times are for one-way travel only and therefore the total time spent travelling should be approximately doubled (i.e., approximately 88 minutes to receive a hospital-based infusion).

After arriving at the hospital to receive ERT, patients reported that therapies were not started immediately but an average 44-minute wait was experienced before ERT, with 42% of patients reporting a >30-minute wait. Following

ERT administration, patients may be required to remain within the healthcare facility for an observation period. All patients reported such a wait period, with an average time of 26 minutes; 42% of patients reported a wait of >30 minutes post-infusion. After the observation period, patients reported an additional wait of an average of 11 minutes prior to discharge due to administrative issues, such as defining the appointment for the next infusion.

Overall, on top of the time required to technically administer ERT, patients are asked on average to secure more than 2 hours and 40 minutes.

A car was the most commonly used means of transport to reach the hospital (n=82). Patients reported an average cost to reach the hospital, per infusion, of €18, which equates to a total annual cost of €68 for patients with Gaucher's or Fabry disease and €36 for patients with MPS-1. This cost included parking fees, public transport fares and any accommodation costs (2 patients required overnight accommodation in a hotel); parking fees were the most frequent cost (57%) but 47% of patients also declared 'other expenses'.

### Home-based enzyme replacement therapy

After receiving the home-based nursing service for ERT for 6 months, 94% of patients believed their lives were better because they were less aware of their health condition (Figure 1a), with 37% and 56% believing their quality of life to be 'greatly improved' and 'improved', respectively (Figure 1b). Most importantly, this positive perception was maintained over time, with almost twice the number of patients considering their quality of life to be 'greatly improved' at 18 months compared with 6 months (60% versus 37% with 99% significance) (Figure 1b).

Figure 1a Patients' perception of the effect of the TuTor service on their health condition

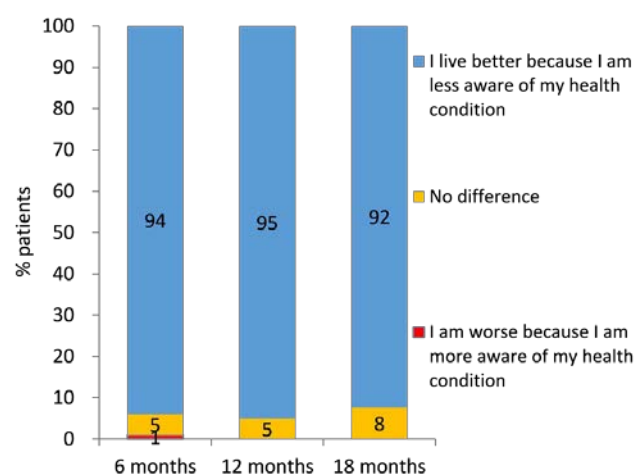
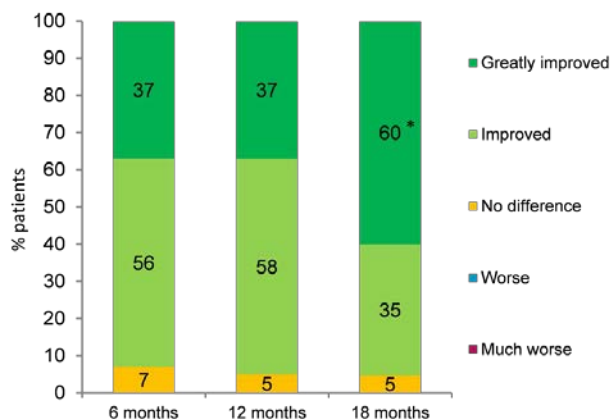


Fig 1b Impact of the TuTutor service on patients' quality of life (\*99% significance compared with 6 months)

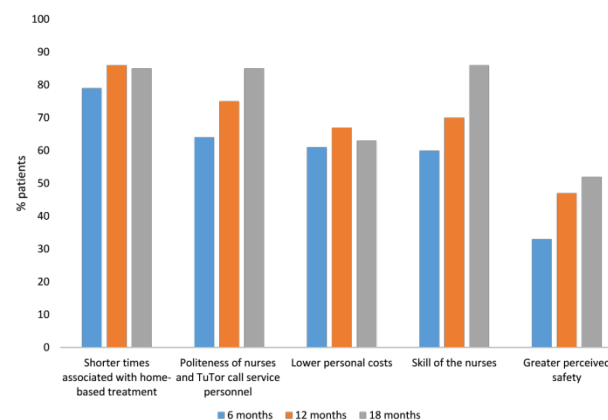


Overall, after receiving the service for 6 months, the skill of the nurses providing the home-based nursing service was considered 'excellent' by 69% of patients and 'good' by 26% of patients, with 83% rating the politeness of the nurses as 'excellent'. At 12 months, the nurses' skill rate was considered 'excellent' by 74% of patients, further increasing to 88% at 18 months.

Similarly, the skill and politeness of the TuTutor call service personnel was considered 'excellent' by 84% and 85% of patients at 6 months, respectively. The high quality of service provided by the TuTutor call service personnel was maintained over time with 86% and 88% of patients rating their skill and politeness as 'excellent' at 18 months, respectively. Infusion therapy at home was considered 'more comfortable and/or relaxing' by almost all patients (98% to 100%) during the 18 month assessment period, 98% to 100% considered that at-home infusion therapy allowed them to save time and/or money and 95% to 98% of patients considered that at-home infusion therapy provided the same professional/safe level of treatment as that offered in a hospital. Very few patients reported missing the hospital setting (4% to 5%), the direct contact with hospital staff (5% to 11%), or the direct contact with other patients (3% to 8%).

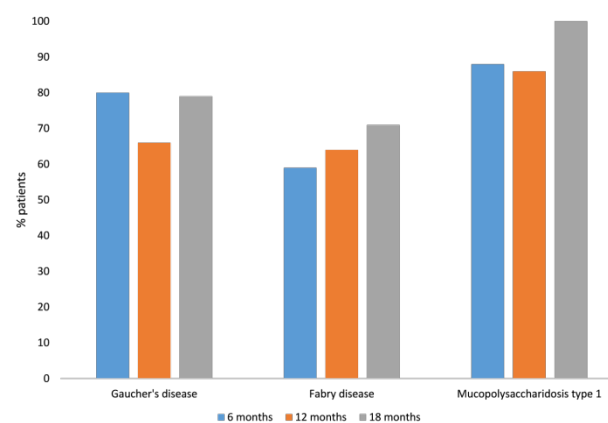
The overall level of satisfaction with the home-based nursing service was rated as 'positive' or 'very positive' by 99% to 100% of patients at all 3 time points. The most important factors behind this positive opinion at 6 months, 12 months and 18 months were ranked as follows: time associated with home-based treatment (79% to 86%), the politeness of the nurses and telephone interviewers (64% to 85%), lower out-of-pocket costs (61% to 67%), the skill of the nurses (60% to 86%) and greater perceived sense of safety (33% to 52%) (Figure 2).

Figure 2 Percentage of patients who rated their satisfaction with the TuTutor service as 'very positive' or 'positive' at 6, 12 and 18 months



When separated into the 3 disease types, the overall level of satisfaction with the home-based nursing service was rated as 'very positive' by the majority of patients (Figure 3). Overall, 99% to 100% of patients reported that they would recommend the home-based nursing service to other patients with their condition.

Figure 3 Percentage of patients with different disease types who rated their experience with the TuTutor service as 'very positive' at 6, 12 and 18 months



## Discussion

For patients with LSDs, receiving intravenous ERT in a hospital-based setting over time can be disruptive of daily activities such as work or study, stressful and inconvenient and may negatively impact their perception of quality of life. This was the rationale behind the development of the TuTutor home-based nursing program that was implemented together with a user experience survey. The current questionnaire-based study has shown a high level of overall patient satisfaction, with 99% to 100% of patients rating this service as 'positive' or 'very positive' at 6 months, 12 months and 18 months. Notably, patients rated the shorter

times associated with home-based treatment to be particularly important. This is unsurprising, since it takes these patients an average of more than 2 hours, in addition to time associated with the infusion, when travelling to receive ERT at a hospital. Furthermore, hospital-based ERT does not just impact on an individual patient's time, since 2 out of 3 patients need the support of a caregiver in order to travel to the hospital.

Irrespective of the therapy/disease covered by the TuTor program, the overall level of satisfaction with this home-based nursing service was similarly high for all three disease types and generally increased over time despite the variation in patient numbers for each pathology. The service appeared to match patients' expectations as well as to be capable to adjust over time: patients with Gaucher's disease reported a decrease in their satisfaction levels at 12 months, which recovered at the 18-month time point. However, due to the low patient numbers when the three groups of patients were analyzed separately, care must be taken when interpreting these results individually.

With the TuTor program, the perception of patients' health was used as a proxy for quality of life. Importantly, this positive perception was maintained over time and across all three patient groups. Overall, the ability to receive infusion therapy at home was a solution welcomed by almost all the patients, with most patients reporting that they would recommend the home-based nursing service to other patients with their condition.

Our results are consistent with previous studies of home-based therapy for lysosomal storage disorders showing that transfer of ERT from the hospital setting to home-based care positively impacts on the perception of quality of life, with home-based therapy shown to fit in better with family schedules and work commitments and result in less stress than travelling to hospital every 2 weeks (or every week for MPS-1) [16,17].

Our results also showed that the nurses involved in the TuTor program and the TuTor call service personnel who supported them, provided a high quality service, which either remained stable or improved over time. The skill of the nursing staff, which was initially rated very well but slightly lower than their politeness or than the skill and politeness of the TuTor call service personnel, improved markedly over time and was rated as 'excellent' by the majority of patients at 18 months. The increase over time in the proportion of patients rating the skill of the nurses as 'excellent' may be a reflection of increased comfort levels of the patient with receiving their infusions at home and feeling more at ease with the nursing staff. One peculiarity of the TuTor program is to match, whenever possible, a specific nurse to a given patient. The decision to match nurse and patient has arisen from the intuition that this may establish a better professional relationship and especially when a patient's infusions are performed by the same nurse.

Finally, the findings of this survey must be considered to be specific to the TuTor nursing service and care must therefore be taken if extrapolating to other nursing services, as the level of patient satisfaction is likely to be significantly influenced by the skill level and politeness of the nurses delivering the service. The findings are also

specific to patients with Gaucher's disease, Fabry disease or MPS-1, but the findings are likely to be applicable to other patients with chronic conditions requiring frequent trips to hospital to receive treatment.

## Conclusion

In patients with LSDs receiving ERT, a home-based nursing service may provide patients with an increase in their perception of quality of life over a hospital-based service, largely due to the time saving and increased convenience associated with such a service.

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