






BRIEF REPORT

REVISED First two years of reimbursed enzyme replacement therapy in the treatment of Fabry disease in Poland [version 2; peer review: 2 approved]

Michał Nowicki ¹, Monika Komar², Mariusz Kuzstal³, Katarzyna Mizia-Stec⁴, Tomasz Liberek⁵, Jolanta Małyszko ⁶, Katarzyna Muras-Szwedziak¹, Krzysztof Pawlaczyk ⁷, Piotr Podolec², Jarosław Sławek⁸

¹Department of Nephrology, Hypertension, and Kidney Transplantation, Medical University of Łódź, Łódź, Poland

²Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College, Cracow, Poland

³Department of Nephrology and Transplantation Medicine, Wrocław Medical University, Wrocław, Poland

⁴1st Department of Cardiology, Silesian Medical University, Katowice, Poland

⁵Department of Nephrology, Transplantation and Internal Medicine, Medical University of Gdańsk, Gdańsk, Poland

⁶Department of Nephrology, Dialysis and Internal Diseases, Medical University of Warsaw, Warsaw, Poland

⁷Department of Nephrology, Transplantation and Internal Medicine, Poznań University of Medical Sciences Karol Marcinkowski, Poznań, Poland

⁸Department of Neurological-Psychiatric Nursing, Medical University of Gdańsk, Gdańsk, Poland

V2 First published: 20 Aug 2021, 10:841
<https://doi.org/10.12688/f1000research.55313.1>
 Latest published: 22 Oct 2021, 10:841
<https://doi.org/10.12688/f1000research.55313.2>

Abstract

Fabry disease (FD) is an ultra-rare genetic lysosomal storage disease caused by pathologic gene variants resulting in insufficient expression of α -galactosidase A. This enzyme deficiency leads to accumulation of globotriaosylceramide and globotriaosylsphingosine in plasma and in different cells throughout the body, causing major cardiovascular, renal, and nervous system complications. Until 2018, reimbursed enzyme replacement therapy (ERT) for FD was available in all European Union countries except Poland.



We present the preliminary results of the first two years of reimbursed ERT in Poland. We obtained data from the seven largest academic centers in Katowice, Cracow, Wrocław, Poznań, Gdańsk, Warsaw, and Łódź. The questionnaire included the following data: number of patients treated, number of patients qualified for ERT, and patient characteristics.

All centers returned completed questionnaires that included data for a total of 71 patients (28 men and 43 women) as of June 2021. Thirty-five patients with the diagnosis of FD confirmed by genetic testing (22 men and 13 women) had already qualified for reimbursed ERT. Mean (SD) age at the commencement of the ERT program was 39.6 (15.5) years (range 18-79 years). Mean time from the first clinical symptoms reported by the patients to the FD diagnosis was 21.1 (8.9)


Open Peer Review

Reviewer Status  

Invited Reviewers

| | 1 | 2 |
|------------------|---|---|
| version 2 | | |
| (revision) |  |  |
| 22 Oct 2021 | report | report |
| |  |  |
| version 1 | | |
| 20 Aug 2021 |  |  |
| | report | report |

1. **Andrzej J. Jaroszynski** , Jan Kochanowski
 University of Kielce, Kielce, Poland

2. **Bojan Vujkovic** , General Hospital Slovenj
 Gradec, Slovenj Gradec, Slovenia

Any reports and responses or comments on the article can be found at the end of the article.

years, and the mean time from the final diagnosis of FD to the beginning of ERT was 4.7 (4.6) years.

FD is still underdiagnosed in Poland. To identify undiagnosed FD patients and to ensure that patients in Poland benefit fully from ERT, implementation of an effective nationwide screening strategy and close cooperation with a network of rare disease centers is advised.

Keywords

Fabry disease, enzyme replacement therapy, ultra-rare disease, α -galactosidase, globotriaosylceramide, globotriaosylsphingosine

Corresponding author: Michał Nowicki (nefro@wp.pl)

Author roles: **Nowicki M:** Conceptualization, Data Curation, Formal Analysis, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; **Komar M:** Data Curation, Investigation, Writing – Review & Editing; **Kusztal M:** Data Curation, Investigation, Writing – Review & Editing; **Mizia-Stec K:** Data Curation, Investigation, Writing – Review & Editing; **Liberek T:** Data Curation, Investigation, Writing – Review & Editing; **Małyszko J:** Data Curation, Investigation, Writing – Review & Editing; **Muras-Szwedziak K:** Data Curation, Investigation, Writing – Review & Editing; **Pawlaczyk K:** Data Curation, Investigation, Writing – Review & Editing; **Podolec P:** Data Curation, Investigation, Writing – Review & Editing; **Sławek J:** Supervision, Writing – Review & Editing

Competing interests: M.N., J.S., M.K (Kusztal), report consultation fees from Takeda and Sanofi Genzyme; M.K (Komar), P.P. report consultation fees from Sanofi Genzyme, M.K (Komar), P.P., M.N., K.P., K. M.-S and J.S. report speaker fees from Sanofi Genzyme, M.N. and M.K. report speaker fees from Amicus Therapeutics.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2021 Nowicki M *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Nowicki M, Komar M, Kusztal M *et al.* **First two years of reimbursed enzyme replacement therapy in the treatment of Fabry disease in Poland [version 2; peer review: 2 approved]** F1000Research 2021, **10**:841 <https://doi.org/10.12688/f1000research.55313.2>

First published: 20 Aug 2021, **10**:841 <https://doi.org/10.12688/f1000research.55313.1>

REVISED Amendments from Version 1

We have updated the first version of our manuscript to address the reviewers' comments, particularly to explain the differences between East and West Poland in term of diagnosed Fabry disease cases and to emphasize the need of family screening and early treatment introduction. We hope that the changes improved the quality of our manuscript.

Any further responses from the reviewers can be found at the end of the article

Introduction

Fabry disease (FD) is an ultra-rare genetic lysosomal storage disease caused by pathologic gene variants resulting in insufficient expression of α -galactosidase A (GLA).¹ This enzyme deficiency leads to accumulation of globotriaosylceramide (GL-3) and its deacylated form, globotriaosylsphingosine (lyso-GL-3), in plasma and in different cells throughout the body. Accumulation of GL-3 and lyso-GL-3 causes major organ damage which leads to multiorgan complications involving the central and peripheral nervous systems, kidney, and heart that decrease the quality of life and shorten lifespan.¹ FD is largely underdiagnosed and diagnosis is most often established only after the symptoms of target organ damage has already occurred. Early diagnosis and introduction of disease-specific treatment is essential to stop the disease progression at early stage and prevent from irreversible tissue and organ damage.

The introduction of enzyme replacement therapy (ERT) in 2001 revolutionized the treatment landscape of FD. Clinical studies have proven the efficacy of ERT in the treatment of FD. Specifically, it has been shown that ERT inhibits the progression of target organ damage and stabilizes or even improves organ function. Therefore, international standards and guidelines recommend ERT as the optimal treatment of FD, although for some patients with amenable mutations, an alternative oral chaperone therapy is also available.^{2,3}

The available ERT treatment currently includes recombinant α -galactosidase A enzymes: agalsidase alfa (Replagal, marketed by Shire) and agalsidase beta (Fabrazyme, marketed by Sanofi Genzyme). In the EU, both agalsidase alfa and agalsidase beta have been approved and available for 20 years. Agalsidase alpha and beta are administered every two weeks by intravenous infusion at a dose of 0.2 mg/kg and 1.0 mg/kg, respectively.^{4,5} Although two ERT preparations are currently available and approved for the treatment of FD, there are ongoing debates as to what dose of agalsidase preparation may offer better target organ protection. Two recent national guidelines suggested that higher doses of the recombinant enzyme may result in better clinical outcomes, at least in males with a classic phenotype.^{6,7}

Until 2018, reimbursed ERT for FD was available in all EU countries except Poland, where only a limited number of patients who participated in clinical trials or compassionate drug use programs received the treatment.⁸ To help patients with FD obtain access to the therapy, emphasize the challenges they face, and gain public attention, the Association of Families with Fabry Disease, with the help of medical professionals and parliament members, initiated several public campaigns such as “Where is Fabry,”⁹ “Who is Fabry,”¹⁰ and “Fabry Disease – a burning problem”.¹¹ After an initial rejection of the application in 2014, the Polish Ministry of Health eventually included ERT for FD to the list of reimbursable drugs in 2019.

Initially, one of the major challenges in the treatment of FD in Poland was a lack of guidelines for diagnosis and management of the disease.¹² In 2020, an interdisciplinary group of Polish clinicians prepared a comprehensive position statement providing practical recommendations for physicians who treat patients with FD. The position statement was approved by the Boards of the Polish Cardiac Society, Polish Society of Inborn Errors of Metabolism, Polish Society of Internal Medicine, Polish Society of Nephrology, and Polish Society of Neurology.¹³

The introduction of the reimbursable ERT was a major step towards the improvement of the quality of life of Polish patients with FD. However, to date, the results of this treatment program in Poland have not been published. The choice of one of the two available recombinant drugs was the sole decision of the treating physician, but patients had to be centrally approved for the participation in the program by a group of rare disease experts.

Methods

In 2021, two years after the introduction of reimbursed ERT therapy for FD in Poland, we designed a short survey to gather data on the FD patients currently treated in rare disease centers. The survey was distributed via e-mail to the FD attending physicians at seven largest academic centers in Katowice, Kraków, Wrocław, Poznań, Gdańsk, Warszawa, and Łódź. The centers were selected based on the number of patients with FD treated. The questionnaire included the following data: number of patients treated, number of patients qualified for ERT, and patient characteristics (gender, age,

Table 1. Number of patients with Fabry disease treated with enzyme replacement therapy in seven major academic centers in Poland.

| Treatment center | Katowice | Poznań | Wrocław | Gdańsk | Kraków | Łódź | Warszawa | Total |
|--|----------|--------|---------|--------|--------|------|----------|-------|
| N of diagnosed patients with FD | 3 | 6 | 14 | 2 | 16 | 28 | 2 | 71 |
| Men | 2 | 3 | 8 | 2 | 6 | 5 | 2 | 28 |
| Women | 1 | 3 | 6 | 0 | 10 | 23 | 0 | 43 |
| N of patients treated with ERT | 1 | 3 | 6 | 2 | 7 | 12 | 2 | 35 |
| Men | 1 | 2 | 6 | 2 | 4 | 5 | 2 | 22 |
| Women | 0 | 1 | 2 | 0 | 3 | 7 | 0 | 13 |

ERT, enzyme replacement therapy; FD, Fabry disease.

date of the qualification to the ERT program, age at the time of qualification, and time from the appearance of the first disease symptoms to the clinical diagnosis).

Data were analyzed using descriptive statistics and Statistica 13.1 PL (StatSoft Polska) software.

Ethics

The following study was non-interventional, questionnaire-based research, therefore, according to local regulations, Ethics Committee approval and patient informed consent were not required. The authors received permission to collect the data from all the centers involved and the patients' personal data were anonymized.

Results

All centers returned completed questionnaires that included data for a total of 71 patients (28 men and 43 women) as of June 2021. Thirty-five patients with the diagnosis of FD confirmed by genetic testing (22 men and 13 women) had already qualified for reimbursed ERT. Mean (SD) age at the commencement of the ERT program was 39.6 (15.5) years (range 18-79 years). The mean time from the final diagnosis of FD to the beginning of ERT was 4.7 (4.6) years, although there was a substantial delay from the first clinical symptoms reported by the patients to the diagnosis - 21.1 (8.9) years. The centers with the largest number of patients with FD was Łódź, Cracow, and Wrocław. Detailed numbers of the patients diagnosed and receiving ERT reported by each center in Poland are provided in [Table 1](#).

Discussion

FD is still underdiagnosed in Poland since the reported disease prevalence and number of patients currently receiving the therapy is lower than in other EU countries. For example, in Germany, the estimated treated FD prevalence was 0.85 per 100,000 insured patients from 2010 to 2017,¹⁴ which when extrapolated to the Polish population, may suggest that there should be at least 300 patients with FD that may require specific treatment. Lack of ERT reimbursement until 2018 seems to be the main cause of lower number of patients diagnosed with FD compared to other European countries, but data on FD incidence before ERT reimbursement are not available. The situation is improving since the survey showed that almost half (48%) of the Polish patients with FD are already on reimbursed ERT therapy. However, our study reflected some disproportion between eastern and western Poland in terms of number of diagnosed FD cases. This might be due to national fund criteria for medical centers that can be contracted for ERT, with only highly specialized facilities being eligible, therefore, some patients need to move to another province to receive treatment. Also, eastern Poland is less populated than western part. On the other hand, our study concerned only seven biggest centers, selected based on the number of patients with FD treated. Therefore, in eastern Poland there may be patients with FD diagnosed and treated, however, the study inclusion criteria did not capture them. Our findings reflect the important role that the program has already played, but much remains to be done to implement an effective nationwide screening strategy to identify undiagnosed FD patients. The screening should particularly concern high-risk groups, i.e., young patients with cardiovascular accidents and family members of patients already diagnosed with FD. Also, a close cooperation with a network of rare disease centers should be established to ensure that patients in Poland benefit fully from ERT.

Data availability

Underlying data

Zenodo: First two years of reimbursed enzyme replacement therapy in the treatment of Fabry's disease in Poland. <https://doi.org/10.5281/zenodo.5163859>.¹⁵

This project contains the following underlying data:

- FD Polska Res Letter FINAL database.xlsx.

Extended data

Zenodo: First two years of reimbursed enzyme replacement therapy in the treatment of Fabry's disease in Poland. <https://doi.org/10.5281/zenodo.5163859>.¹⁶

This project contains the following extended data:

- Copy of survey (translated to English)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

Acknowledgements

The authors would like to thank Proper Medical Writing and Sanofi Genzyme for their editorial support in preparation of this manuscript.

References

1. Germain DP: **Fabry disease**. *Orphanet J Rare Dis*. 2010; **5**: 30.
2. Wanner C, Arad M, Baron R, et al.: **European expert consensus statement on therapeutic goals in Fabry disease**. *Mol Genet Metab*. 2018; **124**: 189–203.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Ortiz A, Germain DP, Desnick RJ, et al.: **Fabry disease revisited: management and treatment recommendations for adult patients**. *Mol Gen Metabol*. 2018; **123**: 416–427.
[PubMed Abstract](#) | [Publisher Full Text](#)
4. **Replagal – Summary of product characteristics**. Accessed June 28, 2021.
[Reference Source](#)
5. **Fabrazyme – Summary of product characteristics**. Accessed June 28, 2021.
[Reference Source](#)
6. Amsterdam UMC: **Protocol Diagnosis, evaluation and treatment of Fabry disease in the Netherlands V**. 2020 Updated by: M. Langeveld, C.E. Hollak, S. Klein van Loon, S. van der Veen, M. el Sayed, E. Eskes
7. Sirrs S, Bichet DG, Iwanochko RM, et al.: **Canadian Fabry Disease Treatment Guidelines 2019**. Oct 2019; **4**: 2019.
8. Spada M, Baron R, Elliott PM, et al.: **The effect of enzyme replacement therapy on clinical outcomes in paediatric patients with Fabry disease: a systematic literature review a European panel of experts**. *Mol Genet Metab*. 2018 [Epub ahead of print].
[PubMed Abstract](#) | [Publisher Full Text](#)
9. **Where is Fabry social campaign video**. Accessed on July 29, 2021.
[Reference Source](#)
10. **Who is Fabry social campaign video**. Accessed on July 29, 2021.
[Reference Source](#)
11. **Fabry Disease – a burning problem**. Accessed on July 29, 2021.
[Reference Source](#)
12. Bazan-Socha S, Kuczia P, Musiał J, et al.: **Fabry disease in Poland**. *Pol Arch Intern Med*. 2018; **128**: 567–568.
[PubMed Abstract](#) | [Publisher Full Text](#)
13. Nowicki M, Bazan-Socha S, Błażejewska-Hyzorek B, et al.: **Enzyme replacement therapy in Fabry disease in Poland: position statement**. *Pol Arch Intern Med*. 2020; **130**: 91–97.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Hilz M, DasMahapatra P, Fan Q, et al.: **PRO100 Evaluation of treatment patterns of Fabry Disease utilizing medical claims analyses of a German sickness fund database**. *Value in Health*. 2020; **23**: 347.
[Publisher Full Text](#)
15. Michal N, Monika K, Mariusz K, et al.: **First two years of reimbursed enzyme replacement therapy in the treatment of Fabry's disease in Poland [Data set]**. *Zenodo*. 2021.
[Publisher Full Text](#)
16. Nowicki M, Komar M, Kusztal M, et al.: **First two years of reimbursed enzyme replacement therapy in the treatment of Fabry's disease in Poland**. 2021.
[Publisher Full Text](#)

Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 01 November 2021

<https://doi.org/10.5256/f1000research.78579.r97666>

© 2021 Vujkovic B. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Bojan Vujkovic 

Centre for Fabry Disease, General Hospital Slovenj Gradec, Slovenj Gradec, Slovenia

I agree with all answers, comments, and changes the authors made. I have no further comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fabry Disease, Chronic Kidney Disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 25 October 2021

<https://doi.org/10.5256/f1000research.78579.r97665>

© 2021 Jaroszynski A. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Andrzej J. Jaroszynski 

Department of Nephrology, Collegium Medicum, Jan Kochanowski University of Kielce, Kielce, Poland

The authors addressed all my concerns.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Nephrology, cardiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 13 September 2021

<https://doi.org/10.5256/f1000research.58878.r92671>

© 2021 Vujkovic B. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Bojan Vujkovic 

Centre for Fabry Disease, General Hospital Slovenj Gradec, Slovenj Gradec, Slovenia

The presenting brief report by Dr. Nowicki and colleagues: "First two years of reimbursed enzyme replacement therapy in the treatment of Fabry disease in Poland" is a very interesting paper showing the importance of available treatment for Fabry disease (FD) patients. According to presenting data, FD patients are managed in the seven largest academic centers in the country. Similar to other countries, also in Poland there is a large time delay from the first clinical sign to the final diagnosis, therefore the authors are correctly pointing out the importance of raising awareness of FD as a rare disease.

I have just a few minor suggestions for the authors:

Introduction

1. (Line 9-10): I suggest emphasizing the importance of early treatment. Namely, disease-specific therapy is efficient only when started before irreversible changes develop. Due to that fact, it is also important to diagnose FD patients at an early age.

Results:

1. If possible, it would be of great interest to also include in the Results data on how many families were affected. Namely according to Laney DA *et al.*¹, family screening is very effective in diagnosing new patients as there were five family members diagnosed for every proband.
2. Table 1: I would suggest renaming the first group of patients ("N of treated patients with FD" to "N of diagnosed patients with FD)", as it is duplicated and misleading. Also, check the numbers of treated patients with ERT - under Wroclaw numbers and sum are not correct. Check also the final sum of treated in the table and also in text.

Discussion:

1. In order to diagnose young patients (i.e. children) and females, the most effective way is family screening. I would suggest adding that fact to the discussion part and explain if it was done or not in Poland. It could be elaborated in a part where you mentioned "effective nationwide screening strategy", which is probably too vague expression and should be

explained.

2. Explain the main reasons or obstacles as to why there are still patients not receiving disease-specific treatment despite it being reimbursed.

References

1. Laney DA, Fernhoff PM: Diagnosis of Fabry disease via analysis of family history. *J Genet Couns.* 2008; **17** (1): 79-83 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fabry Disease, Chronic Kidney Disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 18 Oct 2021

Michał Nowicki, Medical University of Łódź, Łódź, Poland

Dear Prof. Vujkovic,

We are very pleased to find out that our study met your interest. We are thankful to the Editor and Reviewers for their comments and suggestions, which undoubtedly improved the quality of our manuscript. We enclose a revised manuscript with introduced changes highlighted as track changes.

We addressed all the comments as follows:

Introduction

- (Line 9-10): I suggest emphasizing the importance of early treatment. Namely, disease-specific therapy is efficient only when started before irreversible changes develop. Due to that fact, it is also important to diagnose FD patients at an early age.

Author response: Thank you for raising this issue. We emphasized the need for early treatment introduction at the end of the first paragraph: "Early diagnosis and introduction of disease-specific treatment is essential to stop the disease progression at early stage and prevent from unreversible tissue and organ damage."

Results:

- If possible, it would be of great interest to also include in the Results data on how many families were affected. Namely according to Laney DA *et al.*¹, family screening is very effective in diagnosing new patients as there were five family members diagnosed for every proband.

Author response: Unfortunately, we have no data on family connections of the investigated patients—this issue certainly needs to be explored in further research. We emphasized the need for family screening at the end of the Discussion section as follows: "The screening should particularly concern high-risk groups, i.e., young patients with cardio-vascular accidents and family members of patients already diagnosed with FD.". We also suggested screening patients with cardiovascular accidents at an early age due to the fact that this is quite a common symptom of FD bringing patients to emergency department units.

- Table 1: I would suggest renaming the first group of patients ("N of treated patients with FD" to "N of diagnosed patients with FD)", as it is duplicated and misleading. Also, check the numbers of treated patients with ERT - under Wroclaw numbers and sum are not correct. Check also the final sum of treated in the table and also in text.

Author response: Thank you for pointing this out, we have corrected and double-checked the numbers throughout the table and the manuscript.

Discussion:

- In order to diagnose young patients (i.e. children) and females, the most effective way is family screening. I would suggest adding that fact to the discussion part and explain if it was done or not in Poland. It could be elaborated in a part where you mentioned "effective nationwide screening strategy", which is probably too vague expression and should be explained.

Author response: We emphasized the need for family screening at the end of the Discussion section as follows: "The screening should particularly concern high-risk groups, i.e., young patients with cardio-vascular accidents and family members of patients already diagnosed with FD." We also suggested screening patients with cardiovascular accidents at an early age due to the fact that this is quite a common symptom of FD bringing patients to emergency department units.

- Explain the main reasons or obstacles as to why there are still patients not receiving disease-specific treatment despite it being reimbursed.

Author response: To our knowledge, the main reason for some patients not receiving disease-specific FD treatment is the reimbursement criteria, which in Poland are particularly strict. Patients qualify to ERT if they are 8 years or older, have FD confirmed in both genetic

and enzyme activity testing (however, women with evident clinical symptoms can be qualified despite normal galactosidase activity), and if they present with at least one organ complication, attributed to FD in the differential diagnosis. Unfortunately, this excludes patients with asymptomatic FD, diagnosed during family screening.

Competing Interests: No competing interests were disclosed.

Reviewer Report 31 August 2021

<https://doi.org/10.5256/f1000research.58878.r92673>

© 2021 Jaroszynski A. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Andrzej J. Jaroszynski 

Department of Nephrology, Collegium Medicum, Jan Kochanowski University of Kielce, Kielce, Poland

This is a well-written manuscript that reports on the situation of FD patients in Poland two years after the introduction of the ERT reimbursement which enabled the treatment of FD patients in this country. The findings are interesting with some novel data presented regarding the relation between the FD diagnosis and the reimbursement of the ERT. However, the authors should address the following issues:

1. Has there been an increase in the number of diagnoses of FD after the introduction of ERT reimbursement? The lack of reimbursement and hence the lack of therapy may be at least partly the reason why the number of FD diagnosed patients per million of the population is much lower in Poland than in other European countries;
2. The authors should also explain why in the eastern part of Poland patients with FD are not treated/diagnosed. I suggest that these two issues should be discussed in the discussion section.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Nephrology, cardiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 18 Oct 2021

Michał Nowicki, Medical University of Łódź, Łódź, Poland

Dear Prof. Jaroszyński,

We are very pleased to find out that our study met your interest. We are thankful to the Editor and Reviewers for their comments and suggestions, which undoubtedly improved the quality of our manuscript. We enclose a revised manuscript with introduced changes highlighted as track changes.

We addressed all the comments as follows:

- Has there been an increase in the number of diagnoses of FD after the introduction of ERT reimbursement? The lack of reimbursement and hence the lack of therapy may be at least partly the reason why the number of FD diagnosed patients per million of the population is much lower in Poland than in other European countries;

Author response: Thank you for raising this issue. Previous lack of ERT reimbursement indeed seems to be the main cause of the lower number of patients diagnosed with FD compared to other European countries. Unfortunately, we are unable to source the information regarding the number of patients diagnosed with FD before the reimbursement was introduced. We updated the Discussion section accordingly.

- The Authors should also explain why in the eastern part of Poland patients with FD are not treated/diagnosed. I suggest that these two issues should be discussed in the discussion section.

Author response: Indeed, our study suggests some disproportions between eastern and western Poland. This might be due to national fund criteria for medical centers that can be contracted for ERT, with only highly specialized facilities being eligible, therefore, some patients need to move to another province to receive treatment. Also, eastern Poland is less populated than the western part. On the other hand, our study concerned only the seven biggest centers, selected based on the number of patients with FD treated. Therefore, in eastern Poland, there may be patients with FD diagnosed and treated, however, the study inclusion criteria did not capture them. We updated the Discussion section accordingly.

Competing Interests: No competing interests were disclosed.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research