



# Expert Opinion vs Patient Perspective in Treatment of Rare Disorders: Tooth Removal in Lesch-Nyhan Disease as an Example

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**Abstract** Treatment recommendations for rare disorders often are limited by a lack of data from objective clinical trials. As a result, recommendations are often based on expert opinion. Because expert opinions sometimes conflict, many patients turn to the Internet for guidance from others who may have tried a treatment. The increasing numbers of patients and families who post opinions regarding outcomes allow for systematic data collection regarding specific treatments from the patient perspective. We used social media research methods to determine the opinions of family members or other caregivers regarding permanent removal of teeth for treatment of self-injurious biting (SIB) in patients with Lesch-Nyhan disease (LND), a particularly difficult treatment decision where expert opinion is divided. A content analysis of social media postings was used to systematically interpret caregiver posts about tooth extraction from families and other caregivers of patients with LND who posted comments regarding physical or emotional well-being after tooth extraction. A scale was used to rate all posted opinions. Scores ranged from 1 to 5, with 1 being completely negative and 5 being completely positive. 170 comments from 46 unique individuals were collected and scored by two raters. Interrater reliability, determined using a correlation coefficient across all postings, was 0.85, suggesting a high degree of reliability. The overall average caregiver sentiment score was 4.86, which is an overwhelmingly positive endorsement of tooth extraction as a means for controlling SIB. These methods provide a simple strategy for recommending

treatment strategies based on real-world experience when objective clinical trials are unviable.

## Introduction

Many widely used therapeutic interventions for rare disorders are based on limited evidence. Large double-blind placebo-controlled trials that are at the heart of evidence-based medicine are difficult to conduct in rare disorders for many reasons (Bell and Tudur Smith 2014; Griggs et al. 2009). As a result, recommendations for treatments often are based on the opinions of experts. To mitigate the influence of anecdotal experience, there has been an increasing trend for treatment recommendations to be based on consensus statements, which reflect the collective experience of multiple experts. However, experts sometimes fail to reach consensus on critical issues, and consensus statements rarely incorporate the views of patients and their families.

We evaluated the impact of including the views of patients and their families regarding a particularly controversial treatment for Lesch-Nyhan disease (LND), a rare disorder characterized by extreme and repetitive self-injurious biting (SIB) (Anderson and Ernst 1994; Schretlen et al. 2005). SIB is one of the most distressing features of LND for both patients and their families. If untreated, it can lead to self-amputation of digits, serious facial or tongue disfigurement, or life-threatening infections. Experts in pediatrics often recommend a drastic treatment approach that involves tooth extraction, because it is the only reliable means of controlling the behavior (Goodman et al. 2014). On the other hand, dental experts prefer avoiding the permanent cosmetic consequences of tooth removal in a child and recommend various oral appliances such as tooth

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guards or lip protectors (Limeres et al. 2012). Traditional objective clinical trial methodology to address these differences of opinion is not feasible because blinding and placebo controls are impossible. As a result, patients and families are often forced to make their own decisions in the face of conflicting expert opinion.

In this situation, many patients and families seek advice from other patients and families through social media support groups. For LND, patients and their families often post experiences on two Facebook groups. We took advantage of these public resources to methodically collect opinions regarding tooth extraction as a treatment for SIB. These opinions were evaluated by content analysis, a method widely employed in social media research (Snelson 2016).

## Methods

A total of 504 comments posted on two Facebook sites titled *Lesch-Nyhan Syndrome* and *Lesch-Nyhan National Support and Advocacy Group*, before October 27, 2016, were retrieved using the search words “tooth,” “teeth,” and/or “extract.” Two raters independently judged whether each comment qualified as relevant to the topic of tooth extraction in LND. To be included, the comment had to include information regarding the outcome of tooth extraction such as the subject’s physical or emotional well-being, a change in SIB, and/or an opinion regarding the removal of teeth.

Each relevant comment was scored on a scale from 1 to 5, with 1 being strongly negative and 5 being strongly positive specifically regarding tooth extraction for LND

(Table 1). The inter-rater correlation coefficient across all comments was 0.85, suggesting the method for assigning scores was highly reliable. Because some individuals posted the same opinion more than once, all comments were grouped according to the individual posting the comments and averaged to generate a single, general score for each commenter.

## Results

A total of 170 comments from 46 unique posters met criteria for inclusion. Posters made an average of 3.78 comments (SD = 3.03; range = 1–14). In most cases, each posters’ opinions did not change if they commented about tooth extraction more than once, even if they posted many times over the course of several years. Individually, the comments were overwhelmingly positive. Some comments were neutral, but none were strongly negative. The overall score for both rater’s assessments of all commenters’ general scores averaged 4.86 (SD = 0.41; range = 3.13–5).

## Conclusions

These results suggest that patients with LND and their families overwhelmingly endorse tooth extraction as a treatment for SIB in LND. This study focused on a single controversial treatment for a single rare disorder, but the methods are applicable to any treatment for any rare disorder. The methods are simple and inexpensive to apply and offer an alternative to expert opinion from the perspective of patients and their families. The methods also

**Table 1** Scoring of postings

Score	Rater 1	Rater 2	Explanation of score	Example
5	157 (92%)	158 (93%)	Strongly positive comment with no sign of negative viewpoint about tooth extraction	“[He] is doing so well with feeding himself. He has improved so much since he had his teeth removed. Loving the outcome.”
4	8 (5%)	5 (3%)	Mostly positive comment, but commenter endorses a flaw or drawback about tooth extraction	“oh wow. [He] had the top 4 teeth removed so the cheek lip and tongue biting stopped but the right thumb is his now go to. It is so frustrating. If i put a sock on his hand he wont even try but the minute I take it off its like a magnet.”
3	5 (3%)	7 (4%)	Neutral comment or a comment that is equally positive and negative	“We had 4 top teeth removed because of the lip cheek and tongue biting. Now He favors biting just the right hand”
2	0 (0%)	0 (0%)	Mostly negative comment, but commenter endorses a small benefit about tooth extraction	No comments received this score
1	0 (0%)	0 (0%)	Strongly positive comment with no sign of benefit from tooth extraction	No comments received this score

Any personal identifiers were removed and replaced with [He]. A correlation coefficient was used to determine inter-rater-reliability ( $r = 0.85$ )

present some limitations in terms of potential bias. These support groups may not represent all people who underwent tooth extraction, and those with negative opinions might be underrepresented. However, there is no reason to suspect a systematic bias for or against tooth extraction in this situation. Furthermore, generalizable results require a large enough sample size to capture variation among opinions. Only 170 comments from 46 commenters may seem to be a relatively small sample size; however, LND is quite rare, and these numbers are far higher than all studies for any treatment published so far. Even if some patients were represented by multiple posters, they still reflect opinions of different individuals. Finally, conclusions are feasible only if the results are consistently positive or negative. Neutral scores or bimodal distributions of scores would be difficult to interpret. Even with these limitations, the methods seem particularly useful for informing patients regarding treatment recommendations when consensus among experts is lacking, and more objective traditional clinical trial methodology cannot be applied (Gagne et al. 2014).

For future research, it may prove worthwhile to compare the validity of these methods with social media pertaining to other rare diseases. Additionally, there may be utility in exploring the sentiment differences between social media comments and postings to other webpages, such as online discussion forums. Although Facebook was the only website that hosted a sufficient amount of comments for LND, other rare diseases might have a great Internet presence across multiple outlets.

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## Synopsis

Social media research methods provide a simple strategy for recommending treatment strategies based on real-world experience when objective clinical trials are not feasible.

## Details of Contributions of Individual Authors and Corresponding Author

Adam Cotton served as project lead and conducted the initial literature review and organized the methods and analysis. R. B. Bell assisted in the rating of data and review of the manuscript. Dr. H. A. Jinnah, the corresponding

author, supervised the research, helped write the manuscript, and provided general guidance to the researchers.

## Funding and Conflict of Interest

This project was not funded. As such, there were no financial conflicts of interest among any of the authors.

## Competing Interest Statement

The data in this study were not published in any other article. None of the authors had any financial or other compensatory interest associated with this study.

## Compliance with Ethics Guidelines and Patient Consent

This study gathered data from publicly accessible social media posts whose posters willingly published their text knowing that their identifying information was linked to their comments, so informed consent was not required.

## Financial Disclosures Related to the Manuscript

None.

## References

- Anderson LT, Ernst M (1994) Self-injury in Lesch-Nyhan disease. *J Autism Dev Disord* 24:67–81
- Bell SA, Tudur Smith C (2014) A comparison of interventional clinical trials in rare versus non-rare diseases: an analysis of [ClinicalTrials.gov](http://ClinicalTrials.gov). *Orphanet J Rare Dis* 9:170
- Gagne JJ, Thompson L, O'Keefe K, Kesselheim AS (2014) Innovative research methods for studying treatments for rare diseases: methodological review. *BMJ* 349:g6802
- Goodman EM, Torres RJ, Puig JG, Jinnah HA (2014) Consequences of delayed dental extraction in Lesch-Nyhan disease. *Mov Disord Clin Pract* 1:225–229
- Griggs RC, Batshaw M, Dunkle M, Gopal-Srivastava R, Kaye E, Krischer J, Nguyen T, Paulus K, Merkel PA, Rare Diseases Clinical Research Network (2009) Clinical research for rare disease: opportunities, challenges, and solutions. *Mol Genet Metab* 96:20–26
- Limeres J, Feijoo JF, Baluja F, Seoane JM, Diniz M, Diz P (2012) Oral self-injury. An update. *Dent Traumatol* 29:8–14
- Schretlen DS, Ward J, Meyer SM, Yun J, Puig JG, Nyhan WL, Jinnah HA, Harris JC (2005) Behavioral aspects of Lesch-Nyhan disease and its variants. *Dev Med Child Neurol* 47:673–677
- Snelson CL (2016) Qualitative and mixed methods social media research: A review of the literature. *Int J Qual Methods* 15:1609406915624574