Protocol for Cross-sectional Study of Cannabis Interest and/or Usage among patients with Gaucher Disease

I. **Title of the study**

Prevalence and Outcomes of Cannabis use in Gaucher's Disease: A Survey Study of Patients' Clinical Demographics and Disease Approaches

II. **Literature review**

Gaucher's disease (GD) is an autosomal recessive hereditary illness characterized by insufficient β-Glucocerebrosidase enzyme activity and multiple organ affection due to infiltration with macrophages that store the primary substrate, glucocerebroside. Statistically, it has been estimated that GD affects approximately 1 in 40 thousand persons globally [1]. This incidence has been confirmed for Western countries via newborn screening programs. The disease is uniquely prevalent in Jews of Ashkenazi ethnicity with an incidence of 1:850 [2]. In Western countries, the most common Gaucher disease variant is called GD type 1(GD1). This variant, which is very heterogeneous in terms of signs, symptoms and age of onset of overt clinical manifestations, and prognosis without treatment,does not present with neurological manifestations for much of a patient's life [3]. However, development of Parkinsonism sometimes with associated dementia affects up to 10% of affected individuals who survive to 75-80 years of age [4] [5]. The type 2 and 3 variants include the systemic manifestations of GD1 but with early onset of CNS manifestations and often with decreased life expectancy with deaths occurring

in infancy, childhood and adolescence. However, some individuals with GD3 can survive into middle age with appropriate systemic treatment [6].

Since 1991, the standard management of GD is enzyme replacement with pharmacologic recombinant glucocerebrosidases (ERT), a treatment approach that successfully relieves many of the systemic manifestations such as hepatosplenomegaly, anemia and thrombocytopenia. However, many patients continue to be symptomatic despite ERT due to irreversible bone damage that often occurs due to diagnostic delays and late initiation of therapy. Newer oral therapies offer advantages in terms of convenience of administration but are not yet approved for use in children and teenagers. In addition to chronic pain due to skeletal disease, treated patients often complain of severe fatigue and depression that can limit their joy of living and productivity at school or at work [7]. Thus, there is a continuing need for adjunctive therapies ranging from orthopedic interventions, physical and occupational therapy, and pharmacologic treatments[8]. As with many other individuals with chronic pain, the use of opioids in patients with GD is associated with risk for side effects and addiction.

With the legalization of medical cannabis in many states in the USA and in various countries worldwide, and increasing acknowledged recreational use [9], anecdotal information suggests that GD1 patients across the age spectrum are using these products in pursuit of relief for physical pain and/or psychological relief. However, a literature search revealed no evidence supporting either efficacy or safety for cannabis products in patients with GD. Similarly, there are no studies of dose or route or frequency of administration. In anticipation that such studies will be needed

for cannabis to assume a scientifically legitimate role as a prescribed therapy for GD1 patients, annotation of the current prevalence and methodology of cannabis use by GD patients should help in design and prioritization of future research trials. Because we do not know to what extent patients' use of cannabis is documented in standard medical records (and suspect that it is infrequent), we have designed a patient-reported survey that is intended to provide cross-sectional information about the extent GD1 patients have interest and knowledge of cannabis as an adjuvant therapy, the prevalence of cannabis use in the survey population, its role in alleviating symptoms and any safety issues or adverse reactions that have occurred. This survey also seeks patient-reported data about GD1 history, disease complications, and current disease manifestations and treatments.

III.   **Rationale & background information**

- **Why the research needs to be done**

  There is a lack of knowledge regarding the efficacy and safety of cannabis as an adjuvant therapy for GD1. Knowledge of patients' interest in and/or experience with cannabis in GD will help researchers plan and design needed traditional interventional clinical trials.

- **The most relevant studies published on the subject**

  To the best of our knowledge, this is the first survey study among GD patients that assess patients' general characteristics, management plans, and cannabis use.

IV.   **Objectives**

- To characterize survey participants in terms of GD1 general characteristics, clinical history and current status and treatments.

- As a secondary objective, to determine the prevalence of GD-associated Parkinsonism ini the respondent population.

- To report the patients' level of interest in cannabis as an adjuvant therapy

- To evaluate the prevalence of cannabis use among patients diagnosed with GD and assess patient-reported outcomes..

V. Study design & Methodology

- **Type of study**

  Investigator-initiated cross-sectional patient survey

- **Survey population**

  Patients with GD regardless of their gender, ethnicity, health status, or any other specific characteristic will be surveyed. Only GD patients ages 18 and above will be included. The sample size is not limited. The aim is to achieve a broadly representative sample to the greatest extent possible. The expected duration of recruitment is three months.

- **Sampling plan**

  Potential subjects will primarily be identified for contact and elicitation of interest in the survey study by participating GD center site study coordinators under direction of center medical directors or treating physicians. Patients who express interest will be given information as to how to access the survey tool should they so desire. A record of

participation or non-participation will not be maintained by any GD center

or physician office. Additionally, patients who participate in public GD Facebook or similar on-line groups may be contacted directly by the central investigators to inquire if they are interested in receiving the survey instrument or not. A statement of full disclosure that includes an explanation of the survey's components, the purpose of the survey, and that participation is completely voluntary is included at the beginning of the survey. Patients who participate in the survey, regardless of whether or not they complete and submit it, will be offered a modest incentive in the form of a $5 digital gift card for Starbucks or similar stores.

- **Survey area**

International

- **Data collection and management method**

In order to maintain the accuracy and security of the primary data, access will be restricted to the principal investigators and their research assistants. The survey contains several questions such as the demographics of the respondent including age, weight, and height. It also includes questions about the GD history, symptoms, and current treatment regimen. Further and more importantly, it entails questions regarding the use of cannabis for GD and its outcome. The data will be collected over three months to collect as much representative sample as possible, with a possibility of extending that period so as to ensure a minimum sample size of 250 respondents.

VI.   **Data Analysis plan**

Descriptive statistics will be carried out through SPSS software. Firstly, simple summary statistics will be applied to demographic data to characterize and compare the sample population. Secondly, comparisons of the outcome variables will be considered. P-values less than 0.05 will be considered statistically significant.

VII.   **Ethical considerations**

Risks and Confidentiality

For the purpose of facilitating delivery of the digital gift card, the survey tool does collect email addresses. However, a roster of participants versus non-participants will not be recorded. Furthermore, and most importantly, the email addresses will be accessible only by the principal investigators and their research assistants. In all data analyses, no attempt will be made to connect responses to emails. Collection of email addresses is done with full awareness and consent on the part of the respondents. Regarding questions that some respondents may feel uncomfortable answering, an option of "I'd rather not say" is included. Alternatively, respondents are free to discontinue their participation in which case their data will not be collected or stored. In the explanatory letter at the beginning of the survey, participants are informed of an email address through which they can contact the investigators to receive the digital gift card in the event that they decide to terminate their participation and not complete and submit the survey. Accordingly, the investigators do not perceive any significant risks of harm

of any kind associated with this research study. In any written or published

reports, all data will be collated in an anonymized manner and will not be

connected to email addresses or any other identifying information.

VIII. **Funding sources**

Self funded by the researchers.

IX. **Plan for utilization and dissemination of finding**

Written report shared with study participants and GD practitioners and researchers

at their request after publication in a peer-reviewed journal.

X. **Survey instrument**

Timestamp
Email Address
What is your age?
What is your height? (please indicate if you are using feet/inches or meters/centimeters)
What is your weight? (please indicate if you are using lbs or kg)
What is your sex?
What is your race?
Are you Jewish?
Are you of Ashkenazi or Sefardi origin?
In what country do you live?
What state do you live in?
About how old were you when you were diagnosed with Gaucher disease? In
what decade were you diagnosed with Gaucher disease?
Is your Gaucher Disease being treated and/or monitored by a Gaucher disease specialist? What
is the name of the clinic that treats/monitors your Gaucher Disease? (optional)
With which of the following medications are you currently being treated?
What is your bi-weekly dose of ERT infusion?
Do you know how many vials of ERT you are getting each time you get an infusion?
Can you tell us how many units are in each vial?
And how often do you get your infusion?
What is your daily dose of SRT (oral medication)?
For how long have you been receiving (any) medical treatment for your Gaucher Disease? To
what extent did you have the following medical issues BEFORE beginning treatment?
[Enlarged Spleen]
To what extent did you have the following medical issues BEFORE beginning treatment? [Low
Platelet Count]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bleeding Problems]

To what extent did you have the following medical issues BEFORE beginning treatment? [Frequent Fatigue]

To what extent did you have the following medical issues BEFORE beginning treatment? [Breathing problems (or other lung problems)]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone density problems (osteopenia/osteoperosis)]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint pain]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint damage]

To what extent did you have the following medical issues BEFORE beginning treatment? [Prone to bone fractures]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint surgery/ies]

To what extent did you have the following medical issues BEFORE beginning treatment? [Poor peripheral vision]

To what extent did you have the following medical issues BEFORE beginning treatment? [Memory problems]

To what extent did you have the following medical issues BEFORE beginning treatment? [Problems with coordination]

To what extent did you have the following medical issues BEFORE beginning treatment? [Seizures]

To what extent do you CURRENTLY have the following medical issues? [Enlarged Spleen]

To what extent do you CURRENTLY have the following medical issues? [Low Platelet Count] To what extent do you CURRENTLY have the following medical issues? [Bleeding Problems] To what extent do you CURRENTLY have the following medical issues? [Frequent Fatigue] To what extent do you CURRENTLY have the following medical issues? [Breathing problems (or other lung problems)]

To what extent do you CURRENTLY have the following medical issues? [Bone density problems (osteopenia/osteoperosis)]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint pain]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint damage] To what extent do you CURRENTLY have the following medical issues? [Prone to bone fractures]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint surgery/ies]

To what extent do you CURRENTLY have the following medical issues? [Poor peripheral vision] To what extent do you CURRENTLY have the following medical issues? [Memory problems]

To what extent do you CURRENTLY have the following medical issues? [Problems with coordination]

To what extent do you CURRENTLY have the following medical issues? [Seizures]
Do you have Parkinson's disease?

About how old were you when you were diagnosed with Parkinson's disease? In what decade were you diagnosed with Gaucher disease?

What symptoms led to your diagnosis?

Are you taking any of the following medications?

Do you ever use cannabis products (marijuana and/or any of its extractions, e.g. CBD) for medicinal or non-medicinal purposes?

About how old were you when you began using cannabis? (medical or non-medical use) Where have you obtained cannabis in the past year?

About how often do you use cannabis?

How would you describe your use of cannabis?

Is your medical cannabis use to treat your Gaucher Disease symptoms or Parkinson's Disease symptoms?

About how old were you when you began using cannabis medicinally?

Who recommended using cannabis to treat your symptoms?

Which of the following forms of cannabis have you used in the past year?

For which symptoms do you use medical cannabis? (Check all that apply)

What type of cannabis products do you find most effective for treating your symptoms? (check all that apply)

Which chemical composition of cannabis products do you find most effective for treating your symptoms? (Check all that apply)

How does cannabis use affect your symptoms? [Muscle pain]

How does cannabis use affect your symptoms? [Bone pain]

How does cannabis use affect your symptoms? [Joint pain]

How does cannabis use affect your symptoms? [Mobility]

How does cannabis use affect your symptoms? [Fatigue]

How does cannabis use affect your symptoms? [Anxiety]

How does cannabis use affect your symptoms? [Depression]

How does cannabis use affect your symptoms? [Other]

How does cannabis use affect your symptoms? [Breathing problems]

How does cannabis use affect your symptoms? [General Achiness]

How does cannabis use affect your symptoms? [Bleeding problems]

How does cannabis use affect your symptoms? [Seizures]

How does cannabis use affect your symptoms? [Vision problems]

Have you spoken to your doctor about your use of cannabis?

If not, can you please explain why. (optional - skip if not relevant)

How did your physician respond to learning about your cannabis use?

Do you feel sufficiently educated on the following aspects of cannabis usage? [Consumption methods]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Expected effects]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Time to onset of effects]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Duration of effects]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Precautions]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Interactions with other substances]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Regulatory requirements/legal limitations]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Safe and proper storage]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Safe and proper disposal]

Who educated you on the following [Consumption methods]   [Expected effects] [Time to onset of effects] [Duration of effects] [Precautions] [Interactions with other substances] [Regulatory requirements/legal limitations] [Safe and proper storage]   [Safe and proper disposal]

Are you interested in receiving information about how cannabis may be able to help you gain (greater) relief from your symptoms?

To improve medical knowledge of how cannabis can help ameliorate symptoms of Gaucher Disease and/or Parkinson's Disease, we will be conducting further research which will include elements such as developing a specific regimen of cannabis treatment, assigning randomized placebo groups, and analyzing key clinical data such as blood tests, radiology scans, and specific markers of inflammation. Are you interested in considering participation in this study?

If you would like us to send you more information about using cannabis medicinally or participation in our cannabis study, please write your email address.
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XI.   Explanatory disclosures for Participants

Dear Gaucher Disease Patient,

As it has come to our attention that there is growing interest in the GD community regarding the utilization of cannabis products as an adjuvant therapeutic, primarily for symptoms of pain, and that many individuals with GD are already using such products for said purpose; and, insofar as medical applications of cannabis in humans is still very much an emerging science, and there apparently exists a great deal of confusion regarding legality, efficacy, specific chemical compositions, dosage, and more, we believe that it is of great importance to research this matter for the benefit of the GD community.

Accordingly, we have developed this survey so as to gain a clearer picture of what percentage of GD patients are making use of cannabis for medicinal or other

purposes, and what results, if any, they are seeing in terms of effects on their GD symptoms.

Further, it is our intention to eventually draft a document that will provide helpful information and basic recommendations regarding the usage of cannabis for GD and/or GD/PD symptoms, and we believe that this survey is an important, initial step in that direction.

This survey asks detailed personal questions about health matters, and, most specifically about GD history, treatment, current status, and the use of cannabis products and any observed/experienced benefits therefrom.

Participation in this survey is completely voluntary, and participants can opt to terminate their participation at any time. By completing the survey, participants indicate their voluntary consent.

As a token of our appreciation, all participants will receive a $5 Starbucks e-gift card (redeemable in the US, CA, MX, AU, Macau, HK, IE, & UK) or a 20 NIS Buy-Me e-gift card (redeemable in Israel).

This survey is an independent research project. It has not been commissioned by any company or organization, nor has it been sponsored by any industry or interest party.

Individual participant data will be kept strictly confidential. Data generated by this study will only be used in the public forum after the data is collated and fully anonymized, in the form of a peer-reviewed article and/or a summary that will be sent to colleagues and patient participants.

For any questions regarding this survey, please email doctorrobinely@gmail.com
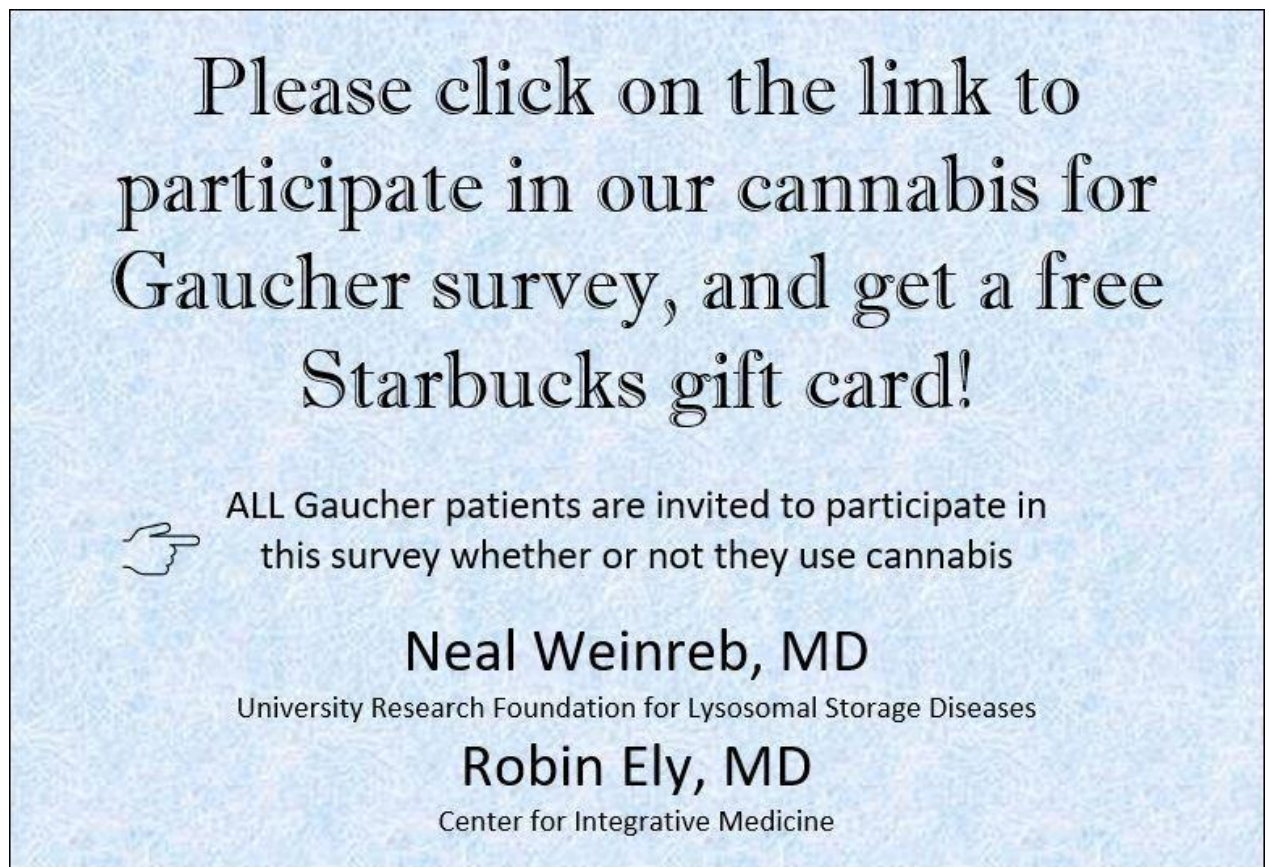
Thank you,

Neal Weinreb, MD

University Research Foundation for Lysosomal Storage Disorders

Robin Ely, MD

Center for Integrative Medicine

XII. Advertisement for Gaucher patient Facebook groups

Please click on the link to participate in our cannabis for Gaucher survey, and get a free Starbucks gift card!

☞ ALL Gaucher patients are invited to participate in this survey whether or not they use cannabis

Neal Weinreb, MD
University Research Foundation for Lysosomal Storage Diseases

Robin Ely, MD
Center for Integrative Medicine

XIII. Recruitment letter to physicians and health care providers who care for patients with Gaucher disease

Dear Colleague,

It has come to our attention that there is a growing interest in the GD community regarding the utilization of cannabis products as an adjuvant therapeutic, primarily for symptoms of pain, and that many individuals with GD are already using such products for said purpose.

Insofar as medical applications of cannabis in humans is still very much an emerging science, there is a great deal of confusion regarding legality, efficacy, specific chemical compositions, dosage, and more. It is our intention to research this matter and, eventually, draft a document that will provide helpful information and basic recommendations for individuals who have access to legally obtained medical cannabis products, regarding the usage of cannabis for GD and/or GD/PD symptoms.

For the initial step of this project, we have created a survey which asks detailed questions about the use of cannabis products, various symptoms, and any observed/experienced benefits.

We would be much obliged if you could inform your GD patients about this survey. Those interested in seeking more information can access the patient explanatory letter which contains a link to the survey at:

https://drive.google.com/file/d/1dyy3bB6xakqfME5wTXvstXUe9F5DuTr_/view?usp=s

haring

Participation is, of course, completely voluntary. The study will be conducted dependent of either a waiver or approval by a National Central Institutional Review Board.

It should be noted that this is an independent research project. It has not been commissioned by any company or organization, nor has it been sponsored by any industry or interest party.

Participant data will be kept strictly confidential. Data generated by this study will only be used in the public forum after the data is collated and fully anonymized, in the form of a peer-reviewed article and/or a summary that will be sent to colleagues and patient participants.

Appreciatively,

Neal Weinreb MD

University Research Foundation for Lysosomal Storage Diseases

Robin Ely MD

Center for Integrative Medicine

XIV. Researchers

- Neal Weinreb, MD, University Research Foundation for Lysosomal Storage Diseases, Boca Raton Florida USA
- Robin Ely, MD, Center for Integrative Medicine.

XV. Declaration of conflicts of interest

The researchers have nothing to declare.

XVI. Contact information

- Neal Weinreb bonneal@hotmail.com

- Robin Ely doctorrobinely@gmail.com

XVII. References

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[8] Giraldo P. Current and Emerging Pharmacotherapy for Gaucher Disease. Clinical Reviews in Bone and Mineral Metabolism. 2019 Dec:1-0.

[9] Hammond D, Goodman S, Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. International Journal of Drug Policy. 2020 Mar:77.

Survey instrument

What is your age?

What is your height? (please indicate if you are using feet/inches or meters/centimeters) What is your weight? (please indicate if you are using lbs or kg)

What is your sex?

What is your race?

Are you Jewish?

Are you of Ashkenazi or Sefardi origin? In what country do you live?

What state do you live in?

About how old were you when you were diagnosed with Gaucher disease? In what decade were you diagnosed with Gaucher disease?

Is your Gaucher Disease being treated and/or monitored by a Gaucher disease specialist? What is the name of the clinic that treats/monitors your Gaucher Disease? (optional)

With which of the following medications are you currently being treated? What is your bi-weekly dose of ERT infusion?

Do you know how many vials of ERT you are getting each time you get an infusion? Can you tell us how many units are in each vial?

And how often do you get your infusion?

What is your daily dose of SRT (oral medication)?

For how long have you been receiving (any) medical treatment for your Gaucher Disease? To what extent did you have the following medical issues BEFORE beginning treatment? [Enlarged Spleen]

To what extent did you have the following medical issues BEFORE beginning treatment? [Low Platelet Count]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bleeding Problems]

To what extent did you have the following medical issues BEFORE beginning treatment? [Frequent Fatigue]

To what extent did you have the following medical issues BEFORE beginning treatment? [Breathing problems (or other lung problems)]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone density problems (osteopenia/osteoperosis)]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint pain]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint damage]

To what extent did you have the following medical issues BEFORE beginning treatment? [Prone to bone fractures]

To what extent did you have the following medical issues BEFORE beginning treatment? [Bone or joint surgery/ies]

To what extent did you have the following medical issues BEFORE beginning treatment? [Poor peripheral vision]

To what extent did you have the following medical issues BEFORE beginning treatment? [Memory problems]

To what extent did you have the following medical issues BEFORE beginning treatment? [Problems with coordination]

To what extent did you have the following medical issues BEFORE beginning treatment? [Seizures]

To what extent do you CURRENTLY have the following medical issues? [Enlarged Spleen] To what extent do you CURRENTLY have the following medical issues? [Low Platelet Count] To what extent do you CURRENTLY have the following medical issues? [Bleeding Problems] To what extent do you CURRENTLY have the following medical issues? [Frequent Fatigue] To what extent do you CURRENTLY have the following medical issues? [Breathing problems (or other lung problems)]

To what extent do you CURRENTLY have the following medical issues? [Bone density problems (osteopenia/osteoperosis)]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint pain]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint damage] To what extent do you CURRENTLY have the following medical issues? [Prone to bone fractures]

To what extent do you CURRENTLY have the following medical issues? [Bone or joint surgery/ies]

To what extent do you CURRENTLY have the following medical issues? [Poor peripheral vision] To what extent do you CURRENTLY have the following medical issues? [Memory problems]

To what extent do you CURRENTLY have the following medical issues? [Problems with coordination]

To what extent do you CURRENTLY have the following medical issues? [Seizures] Do you have Parkinson's disease?

About how old were you when you were diagnosed with Parkinson's disease? In what decade were you diagnosed with Gaucher disease?

What symptoms led to your diagnosis?

Are you taking any of the following medications?

Do you ever use cannabis products (marijuana and/or any of its extractions, e.g. CBD) for medicinal or non-medicinal purposes?

About how old were you when you began using cannabis? (medical or non-medical use) Where have you obtained cannabis in the past year?

About how often do you use cannabis?

How would you describe your use of cannabis?

Is your medical cannabis use to treat your Gaucher Disease symptoms or Parkinson's Disease symptoms?

About how old were you when you began using cannabis medicinally? Who recommended using cannabis to treat your symptoms?

Which of the following forms of cannabis have you used in the past year? For which symptoms do you use medical cannabis? (Check all that apply)

What type of cannabis products do you find most effective for treating your symptoms? (check all that apply)

Which chemical composition of cannabis products do you find most effective for treating your symptoms? (Check all that apply)

How does cannabis use affect your symptoms? [Muscle pain] How does cannabis use affect your symptoms? [Bone pain] How does cannabis use affect your symptoms? [Joint pain] How does cannabis use affect your symptoms? [Mobility] How does cannabis use affect your symptoms? [Fatigue] How does cannabis use affect your symptoms? [Anxiety] How does cannabis use affect your symptoms? [Depression] How does cannabis use affect your symptoms? [Other]

How does cannabis use affect your symptoms? [Breathing problems] How does cannabis use affect your symptoms? [General Achiness] How does cannabis use affect your symptoms? [Bleeding problems] How does cannabis use affect your symptoms? [Seizures]

How does cannabis use affect your symptoms? [Vision problems] Have you spoken to your doctor about your use of cannabis?

If not, can you please explain why. (optional - skip if not relevant) How did your physician respond to learning about your cannabis use?

Do you feel sufficiently educated on the following aspects of cannabis usage? [Consumption methods]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Expected effects] Do you feel sufficiently educated on the following aspects of cannabis usage? [Time to onset of effects]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Duration of effects]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Precautions]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Interactions with other substances]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Regulatory requirements/legal limitations]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Safe and proper storage]

Do you feel sufficiently educated on the following aspects of cannabis usage? [Safe and proper disposal]

Who educated you on the following [Consumption methods]   [Expected effects] [Time to onset of effects] [Duration of effects] [Precautions] [Interactions with other substances] [Regulatory requirements/legal limitations]   [Safe and proper storage]   [Safe and proper disposal]

Are you interested in receiving information about how cannabis may be able to help you gain (greater) relief from your symptoms?

To improve medical knowledge of how cannabis can help ameliorate symptoms of Gaucher Disease and/or Parkinson's Disease, we will be conducting further research which will include elements such as developing a specific regimen of cannabis treatment, assigning randomized placebo groups, and analyzing key clinical data such as blood tests, radiology scans, and specific markers of inflammation. Are you interested in considering participation in this study? If you would like us to send you more information about using cannabis medicinally or participation in our cannabis study, please write your email address

Table 1S: Anthropometric and treatment status of 159 GD patients who completed the survey compared to participants in two ICCG Registry studies with a large representation from the US.

		Cannabis (n=159)		ICGG[a] (n=1028)	ICGG[b] n=2123
Age at diagnosis	**Median age (y)**	12.5		26.8	21.3
Median age (y) (Range)		**145**	**45 (19-80)**	**44.5 (18-85)**	**49.5 (0.8-96.6)**
Characteristics	**Categories**	**Number**	**Percent**	**Percent**	**Percent**
Sex	Female	114	71.7	52.1	53.8
	Male	44	27.7	47.9	46.2
	Preferred not to disclose	1	0.7		
Jewish	Yes	80	50.3	47.3*	60.1
	No	59	37.1		23.9
	Not sure	17	10.7		16.0
	Preferred not to disclose	3	1.9		
Jewish Ethnicity	Ashkenazi	73	45.9		57.0
	Both	2	1.3		2.1
	Not sure	2	1.3		8.3
	Sephardi	2	1.3		1.0
	Not reported	79	49.7		8.7
Country	USA	129	81.1	100	66.4
	Israel	8	5.0		?
	England	6	3.8		
	Canada	4	2.5		
	Australia	4	2.5		0.7
	Others	7	4.3		30.4
Are you treated by a GD specialist?	Yes	145	91.2		
	No	14	8.8		
Do you have Parkinson's Disease?	No	144	90.6		
	Not sure	15	9.4		
Medications in use at the time of the survey	Imiglucerase	49	30.8		
	Velaglucerase	38	23.9		
	alfa	7	4.4		

	Taliglucerase alfa	49	30.8	
	Eliglustat			
	Miglustat	2	1.3	
	Discontinued treatment	7	4.4	
	Never treated	7	4.4	

*Estimated based on percentage of subjects homozygous for N370S genotype. This estimate may exclude Jewish patients with other genotypes (eg. N370S/84GG, N370S/IVS[2+1], N370S/L444P). It may also include some non-Jewish patients homozygous for N370S although is possible that some of these have unknown Jewish ancestry.

[a]Mistry PK, et al. Transformation in pretreatment manifestations of Gaucher disease type 1 during two decades of alglucerase/imiglucerase enzyme replacement therapy in the International Collaborative Gaucher Group (ICGG) Gaucher Registry. Am J Hematol. 2017 Sep;92(9):929-939. doi: 10.1002/ajh.24801.

[b]Rosenbloom BE, et al. Cancer risk and gammopathies in 2123 adults with Gaucher disease type 1 in the International Gaucher Group Gaucher Registry. Am J Hematol. 2022 Oct;97(10):1337-1347. doi: 10.1002/ajh.26675.

Table 2S: Reported symptoms of GD before and following initiation of standard treatment (ERT/SRT) among the respondent GD patients (N=159)
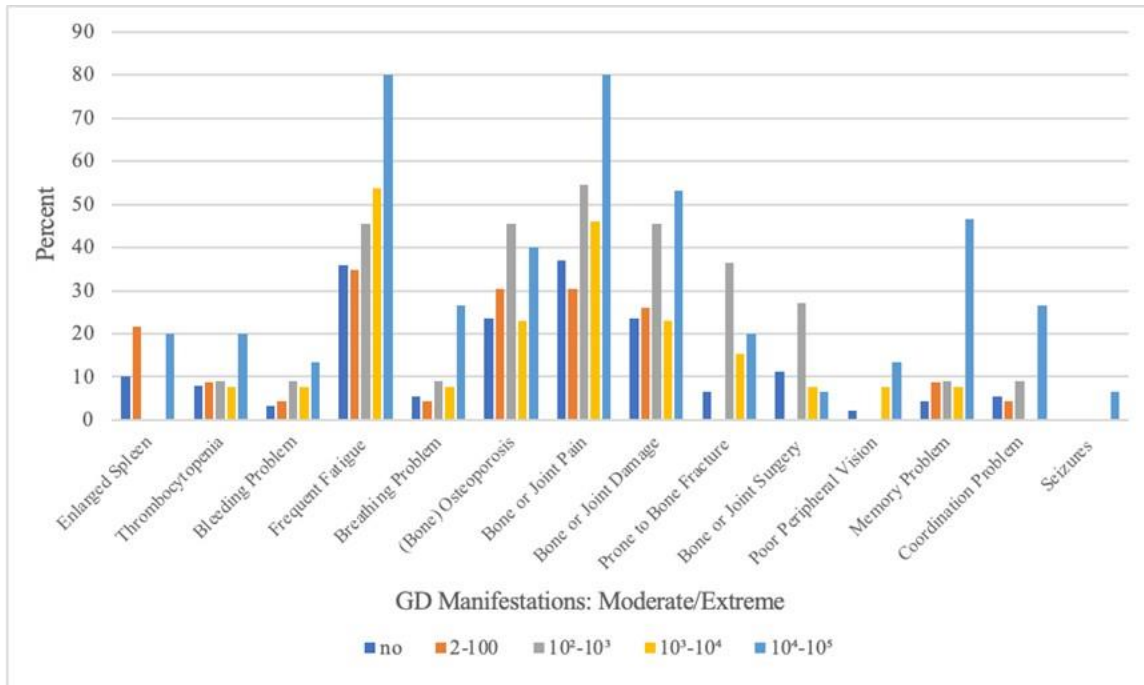
Reported symptoms of GD	Before treatment initiation $_{(t0)}$ At time of response to survey $_{(tr)}$				
	Not at all #(%)	Not sure #(%)	mild #(%)	Moderate #(%)	Extreme #(%)
Enlarged spleen$_{t0}$	11(7.4)	3 (2.0)	30 (20.3)	36(24.3)	68 (45.9)
Enlarged spleen$_{tr}$	85 (53.5)	3 (1.9)	53 (33.3)	12 (7.5)	6 (3.8)
Platelet count$_{t0}$	12 (8.1)	9(6.1)	23 (15.5)	45(30.4)	59 (39.9)
Platelet count$_{tr}$	88 (55.3)	5 (3.1)	52 (32.7)	7 (4.4)	7 (4.4)
Bleeding$_{t0}$	33 (22.3)	7(4.7)	32(21.6)	40(27.0)	36 (24.3)
Bleeding$_{tr}$	101 (63.5)	1 (0.6)	49 (30.8)	5((3.1)	3 (1.9)
Fatigue$_{t0}$	20 (13.5)	4(2.7)	19 (12.8)	46 (31.1)	59 (39.9)
Fatigue$_{tr}$	40 (25.2)	0 (0.0)	51 (32.1)	51 (32.1)	17 (10.7)
Breathing$_{t0}$	105 (70.9)	8(5.4)	18 (12.2)	14 (9.5)	3 (2.0)

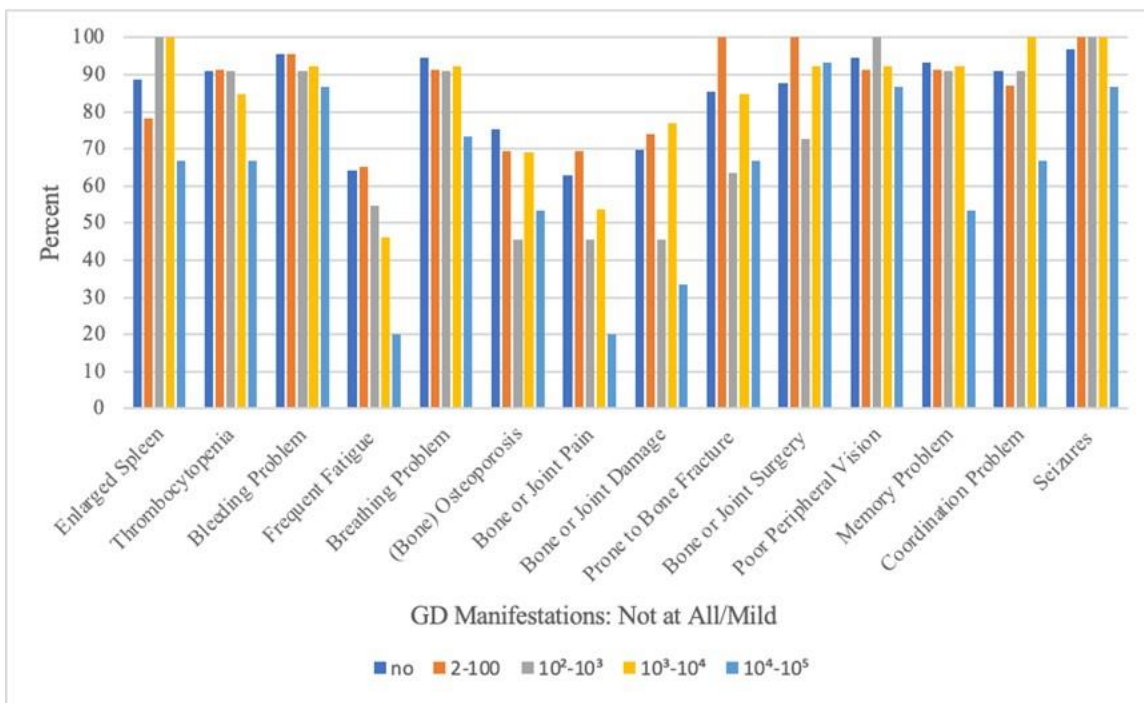|					
Breathing$_{tr}$	123 (77.4)	1 (0.6)	21 (13.2)	9 (5.7)	5 (3.1)
Osteoporosis$_{t0}$	38 (25.7)	17(11.5)	35 (23.6)	37 (25.0)	21 (14.2)
Osteoporosis$_{tr}$	62 (39.0)	5 (3.1)	48 (30.2)	39 (24.5)	5 (3.1)
Joint pain$_{t0}$	29 (19.6)	1 (0.7)	36 (24.3)	44 (29.7)	38 (25.7)
Joint pain$_{tr}$	38 (23.9)	0 (0.0)	54 (34.0)	47 (29.6)	20 (12.6)
Joint damage$_{t0}$	57 (38.5)	10 (6.8)	31 (20.9)	29 (19.6)	21 (14.2)
Joint damage$_{tr}$	65 (40.9)	10 (6.3)	39 (24.5)	32 (20.1)	13 (8.2)
Fracture$_{t0}$	88 (59.5)	12 (8.1)	23 (15.5)	15 (10.1)	10 (6.8)
Fracture$_{tr}$	109 (68.6)	9 (5.7%)	25 (15.7)	12 (7.5)	4 (2.5)
Surgeries$_{t0}$	112 (75.7)	4 (2.7)	13 (8.8)	12 (8.1)	7 (4.7)
Surgeries$_{tr}$	128 (80.5)	1 (0.6)	14 (8.8)	9 (5.7)	7 (4.4)
Vision problem$_{t0}$	116 (78.4)	10 (6.8)	15 (10.1)	6 (4.1)	1 (0.1)
Vision problem$_{tr}$	128 (80.5)	5 (3.1)	19 (11.9)	5 (3.1)	2 (1.3)
Memory problem$_{t0}$	106 (71.6)	4 (2.7)	29 (19.6)	6 (4.1)	3 (2.0)
Memory problem$_{tr}$	90 (56.6)	2 (1.3)	50 (31.4)	13 (8.2)	4 (2.5)
Coordination$_{t0}$	113 (76.4)	7 (4.7)	20 (13.5)	6 (4.1)	2 (1.4)
Coordination$_{tr}$	118 (74.2)	6 (3.8)	22 (13.8)	11 (6.9)	2 (1.3)
Seizures$_{t0}$	139 (93.9)	2 (1.4)	6 (4.1)	0 (0.0)	1 (0.7)
Seizures$_{tr}$	148 (93.1)	4 (2.5)	6 (3.8)	1 (0.6)	0 (0.0)

Table 3S. Symptomatic differences between patients using cannabis products and those not using such products (expressed as percentages) and sub-grouped based on total cannabis days.

Current symptoms	Not sure					Not at all/Mild (percentage)					Moderate/Extreme (Percentage)				
Using Cannabis/total cannabis days	no	"2-100	"10^2-10^3	"10^3-10^4	"10^4-10^5	no	"2-100	"10^2-10^3	"10^3-10^4	"10^4-10^5	no	"2-100	"10^2-10^3	"10^3-10^4	"10^4-10^5
	N=98	N=23	N=11	N=13	N=15	N=98	N=23	N=11	N=13	N=15	N=98	N=23	N=11	N=13	N=15
Enlarged Spleen	1	0	0	0	13	89	78	100	100	67	10	22	0	0	20
Thrombocytopenia	1	0	0	8	13	91	91	91	85	67	8	9	9	8	20
Bleeding Problem	1	0	0	0	0	96	96	91	92	87	3	4	9	8	13
Frequent Fatigue	0	0	0	0	0	64	65	55	46	20	36	35	45	54	80
Breathing Problem	0	4	0	0	0	94	91	91	92	73	6	4	9	8	27
(Bone) Osteoporosis	1	0	9	8	7	75	70	45	69	53	24	30	45	23	40
Bone or Joint Pain	0	0	0	0	0	63	70	45	54	20	37	30	55	46	80
Bone or Joint Damage	7	0	9	0	13	70	74	45	77	33	24	26	45	23	53
Prone to Bone Fracture	8	0	0	0	13	85	100	64	85	67	7	0	36	15	20
Bone or Joint Surgery	1	0	0	0	0	88	100	73	92	93	11	0	27	8	7
Poor Peripheral Vision	3	9	0	0	0	94	91	100	92	87	2	0	0	8	13
Memory Problem	2	0	0	0	0	93	91	91	92	53	5	9	9	8	47
Coordination Problem	3	9	0	0	7	91	87	91	100	67	6	4	9	0	27
Seizures	3	0	0	0	7	97	100	100	100	87	0	0	0	0	7

Figure 1S A

Figure 1S B

Figure 1S. Percentage of patients reporting GD-related signs or symptoms at the time of completion of the questionnaire. For each symptom or sign, the patient cohort is stratified by estimation of total cannabis exposure from the cannabis start date until the questionnaire completion data (lifetime

cannabis days). The calculation was based on the reported frequency of use reported by the patient. However, it is unknown to what extent that frequency was constant over the entire period of cannabis use. A. Patients reporting signs or symptoms of moderate-extreme severity. B. Patients reporting either no signs or symptoms or those reported as mild. The numbers of patients in each cannabis exposure cohort: No cannabis use: 98; 2-100 lifetime cannabis days: 23; 10^2-10^3 lifetime cannabis days: 11; 10^3-10^4 lifetime cannabis days: 13; 10^4-10^5 lifetime cannabis days: 15.