

KNOWLEDGE AND ATTITUDES OF PARKINSON DISEASE RISK IN THE GAUCHER POPULATION*

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Individuals with *GBA* mutations are at an increased risk of developing Parkinson disease

- Gaucher disease
 - AR condition caused by defect in glucocerebrosidase
 - Type 1 is most common, considered non-neuronopathic
 - Symptoms can include bone disease, hepatosplenomegaly, anemia
- Parkinson disease
 - Second-most-common neurodegenerative disorder
 - Loss of dopaminergic neurons in substantia nigra, accumulation of α -synuclein
 - Symptoms can include tremor, rigidity, sleep disturbances

What is the connection between GD and PD?

- “Although the specific contribution of mutant GBA to the pathogenesis of parkinsonism remains unknown, evidence suggests both loss of function and toxic gain-of-function by abnormal β -glucocerebrosidase may be important, and a close relationship between β - glucocerebrosidase and α -synuclein.” –Swan and Saunders-Pullman 2013
- “Patients with GD and GBA heterozygotes have an increased age-specific risk for PD compared with control individuals, with a similar magnitude of PD risk by 80 years of age...” –Alcalay et al. 2014
- “...mild and severe heterozygous GBA mutations differentially affect the risk and the AAO of PD.” –Gan-Or et al. 2015

What have past studies shown?

- “Patients with PD have a high level of interest in genetics and genetic testing, but as an overall group, demonstrate a low level of genetics knowledge.—Falcone et al. 2010
- “Based on experience in a large Parkinson disease research project in which hundreds of carriers of GBA mutations have been identified and counseled, there is indication that there may be insufficient knowledge and awareness about the association of Gaucher and Parkinson disease among patients.” — Cook and Schulze 2017
- “...a survey was administered to individuals who screened negative for GBA mutations.... 86.7% believed that patients should be informed about the increased risk of PD prior to having GD carrier screening...” —Mulhern et al. 2017



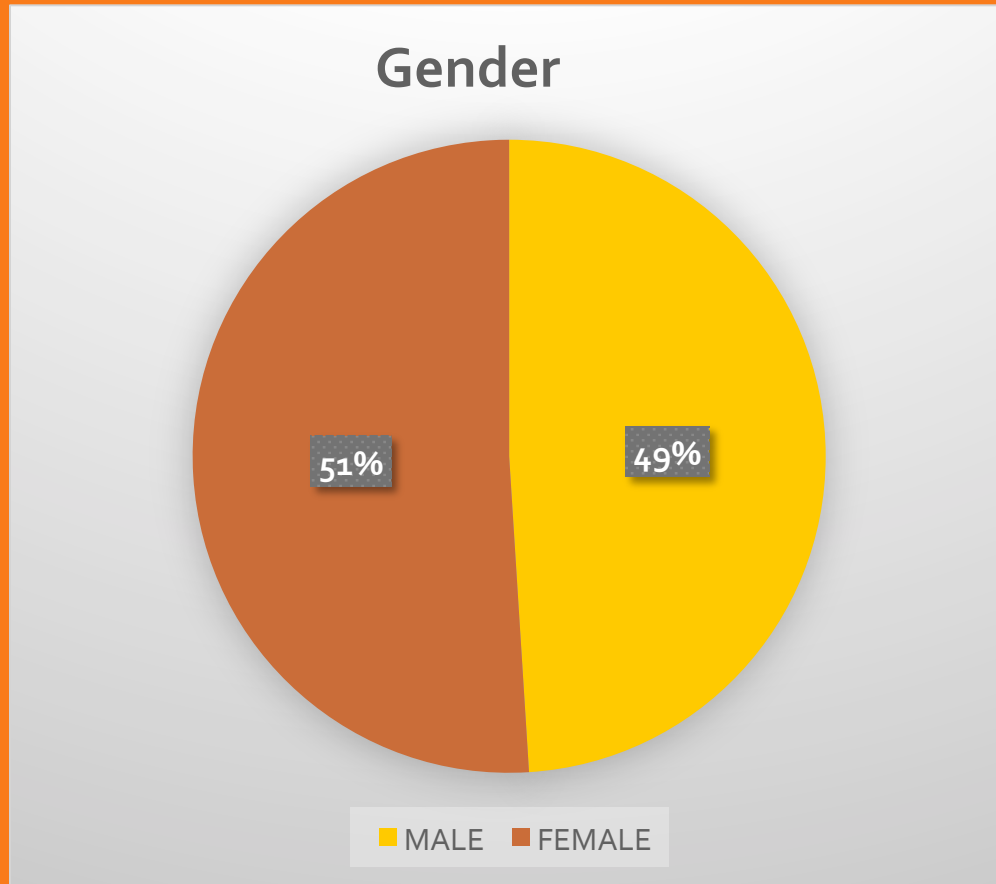
Gaucher Today

- IRB-exempt 24 question survey on SurveyMonkey
 - Demographics
 - Gaucher details
 - Assessment of knowledge regarding Gaucher disease
- Gaucher disease patients 18+ - ISMMS via emails and in clinic, National Gaucher Foundation via monthly electronic newsletter
 - ISMMS total n=76
 - NGF total n=49
- Statistical analysis using Excel and SPSS
 - Analysis of two recruitment groups separately and together

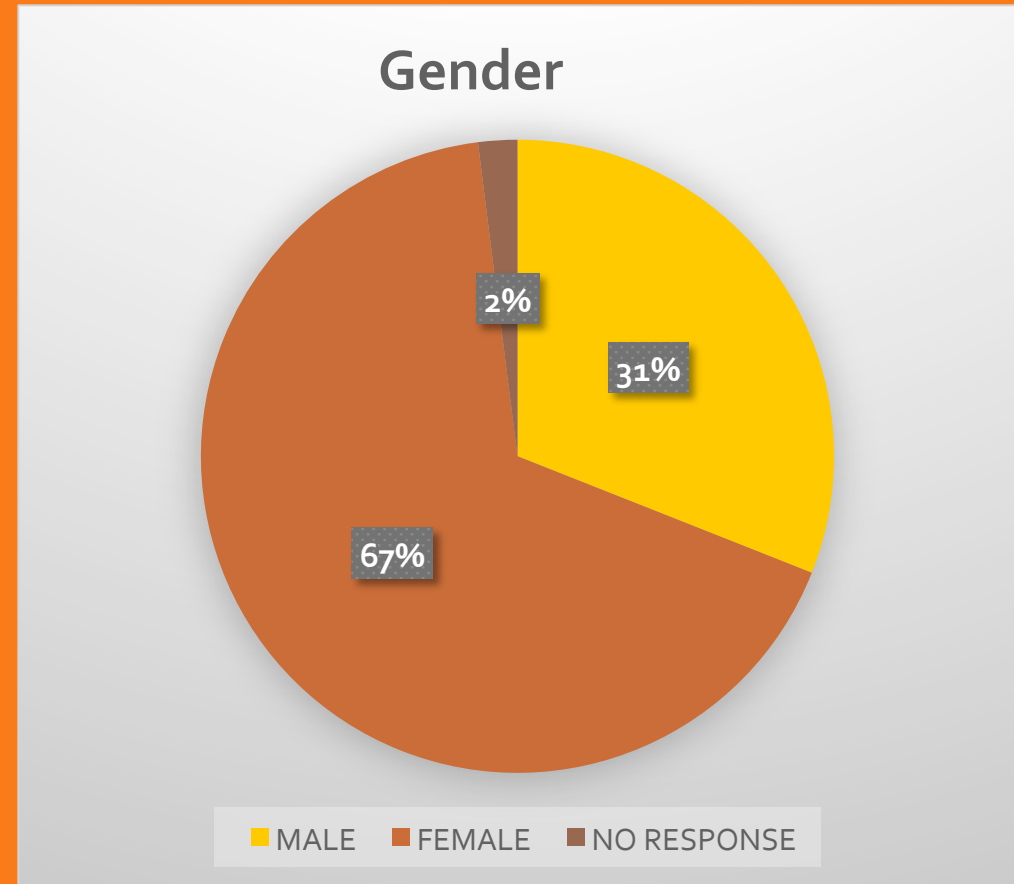
DEMOGRAPHICS



Mount Sinai participants were equally split between male and female, while NGF participants were mostly female

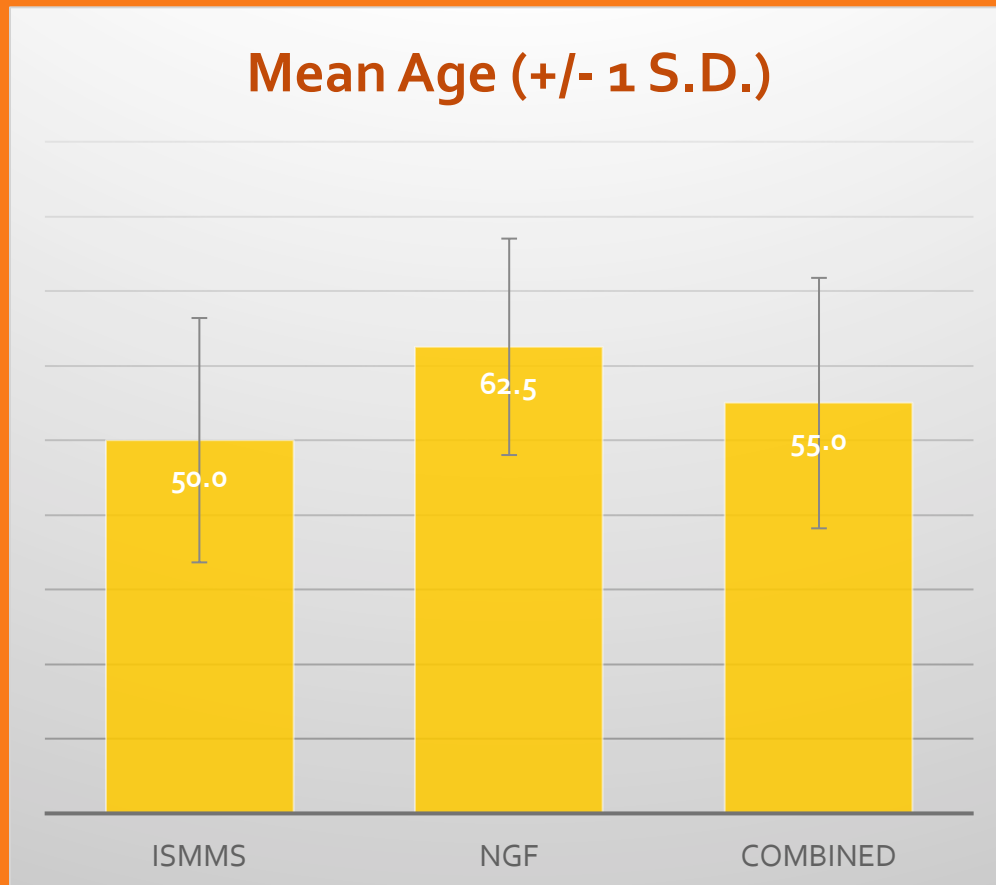


ISMMS n=76



NGF n=49

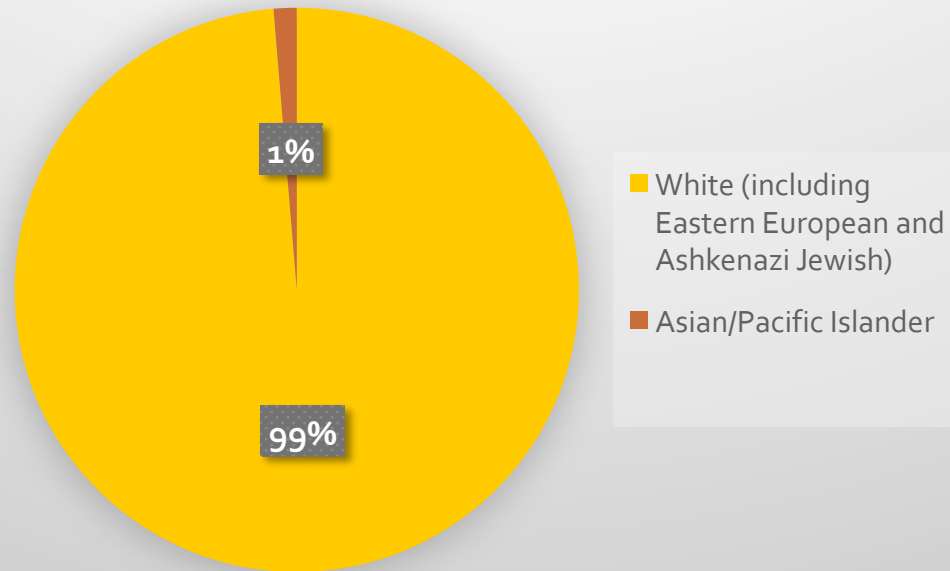
The average Mount Sinai participant was 50 years of age, while the average NGF participant was 62.5 years of age



- ISMMS n=76
 - Average age=50 years
 - Standard deviation=16.4 years
- NGF n=49
 - Average age=62.5 years
 - Standard deviation=14.5 years
- Combined n=125
 - Average age=55.0 years
 - Standard deviation=16.8 years

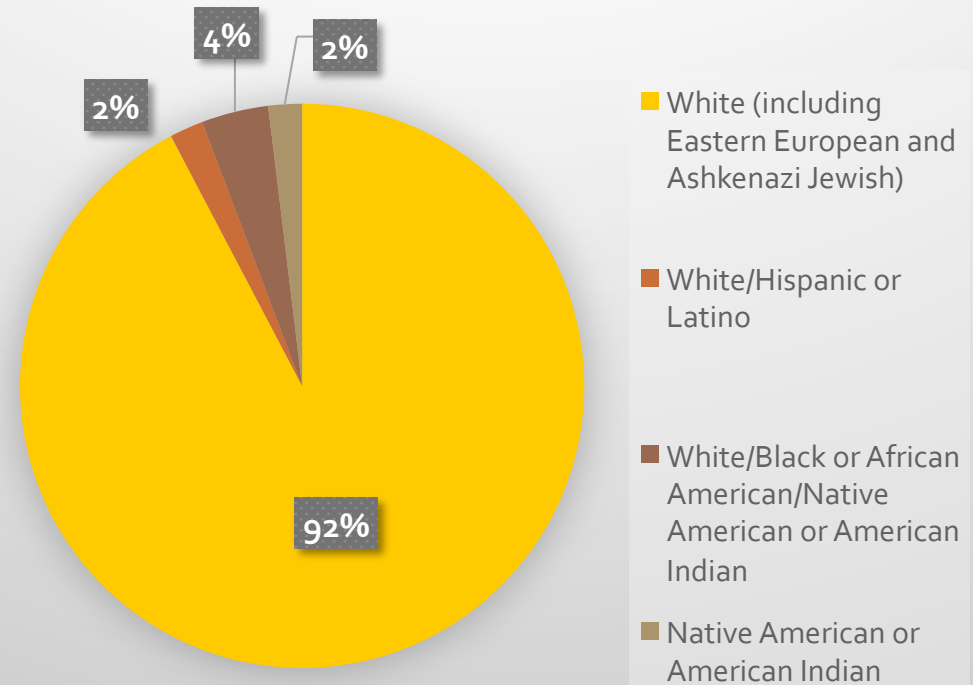
A large majority of participants identified as White, including Eastern European and Ashkenazi Jewish

Ethnicity



ISMMS n=76

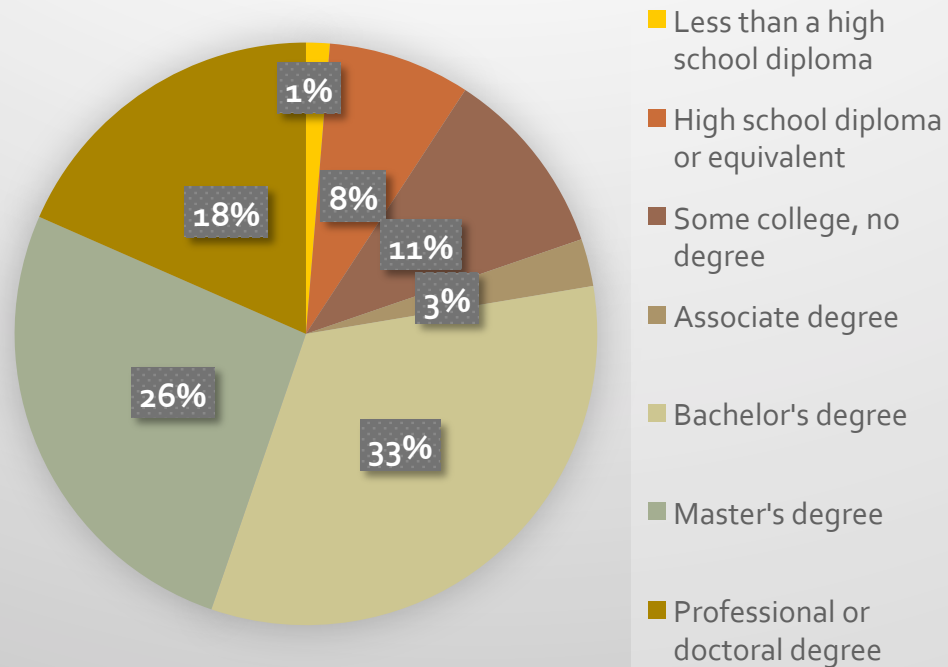
Ethnicity



NGF n=49

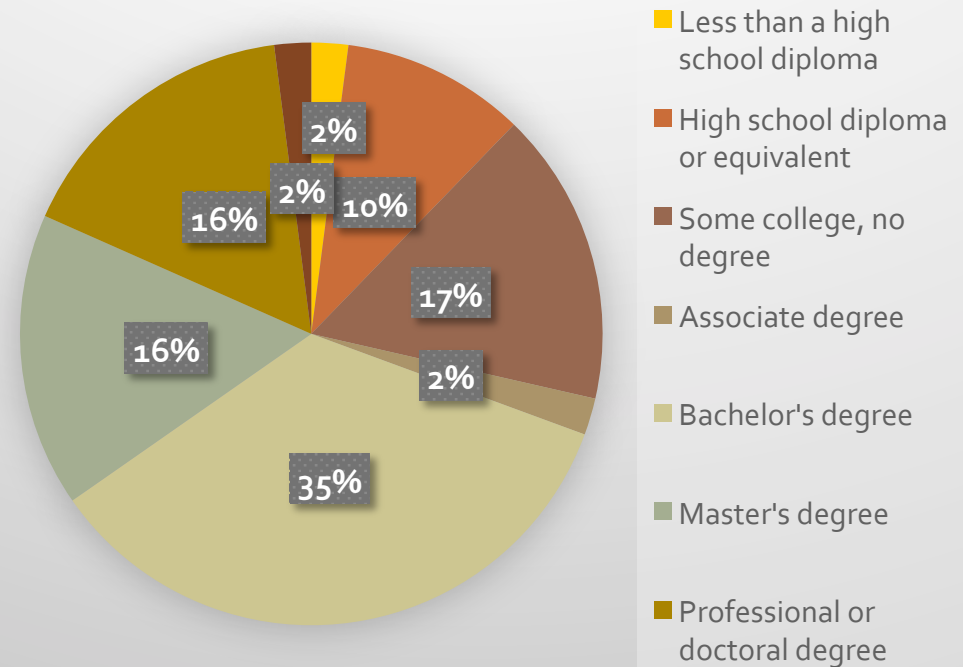
Overall, around 74% of participants had at least a bachelor's degree

Education



ISMMS n=76

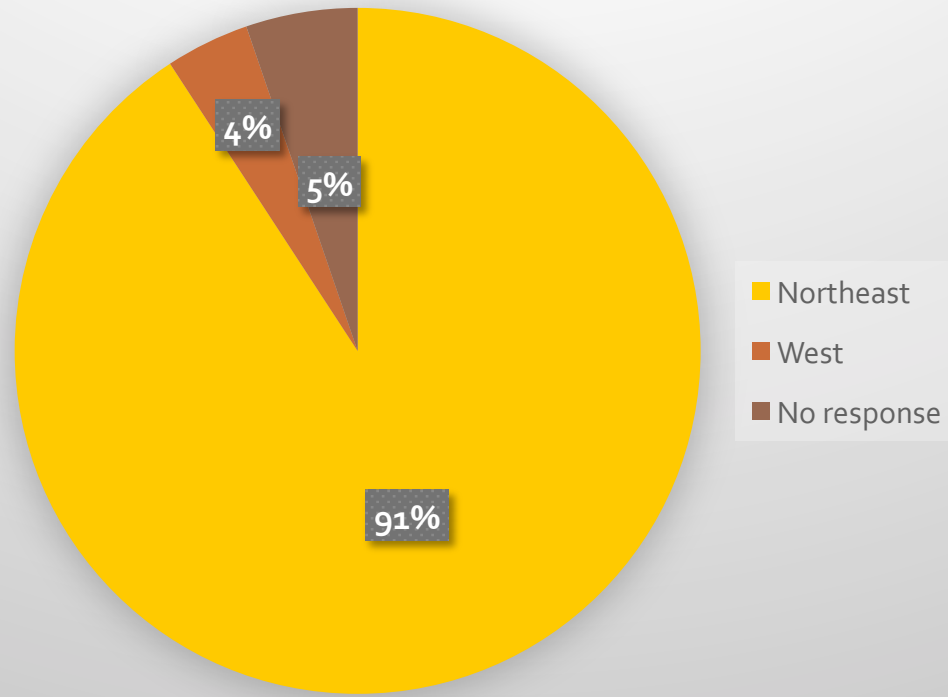
Education



NGF n=49

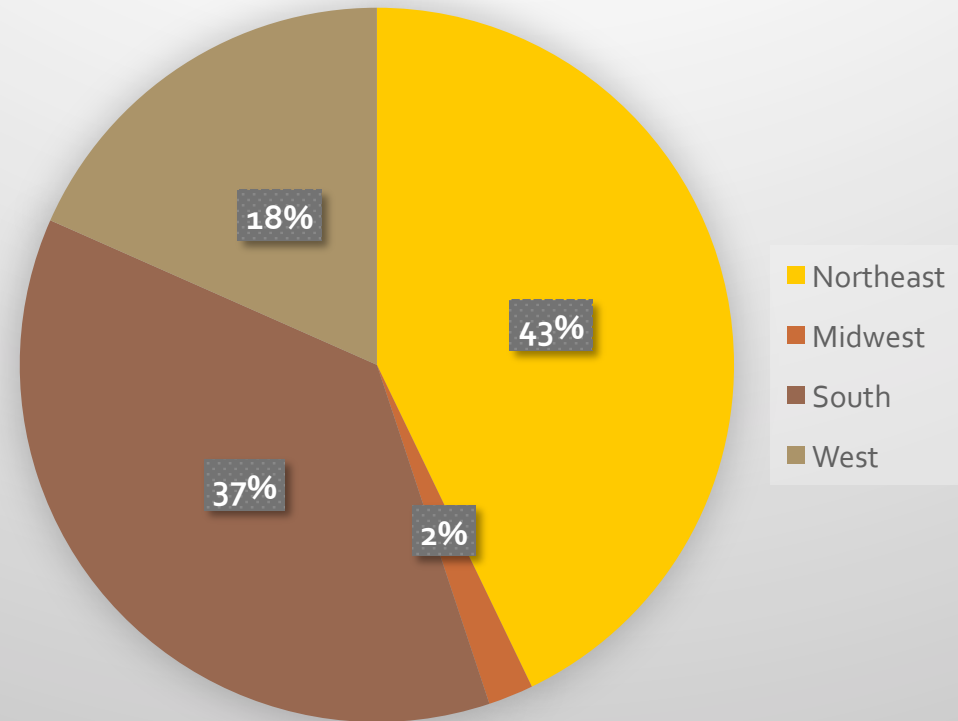
Overall, participants hailed from 18 states, with a majority living in New York and New Jersey

Residence

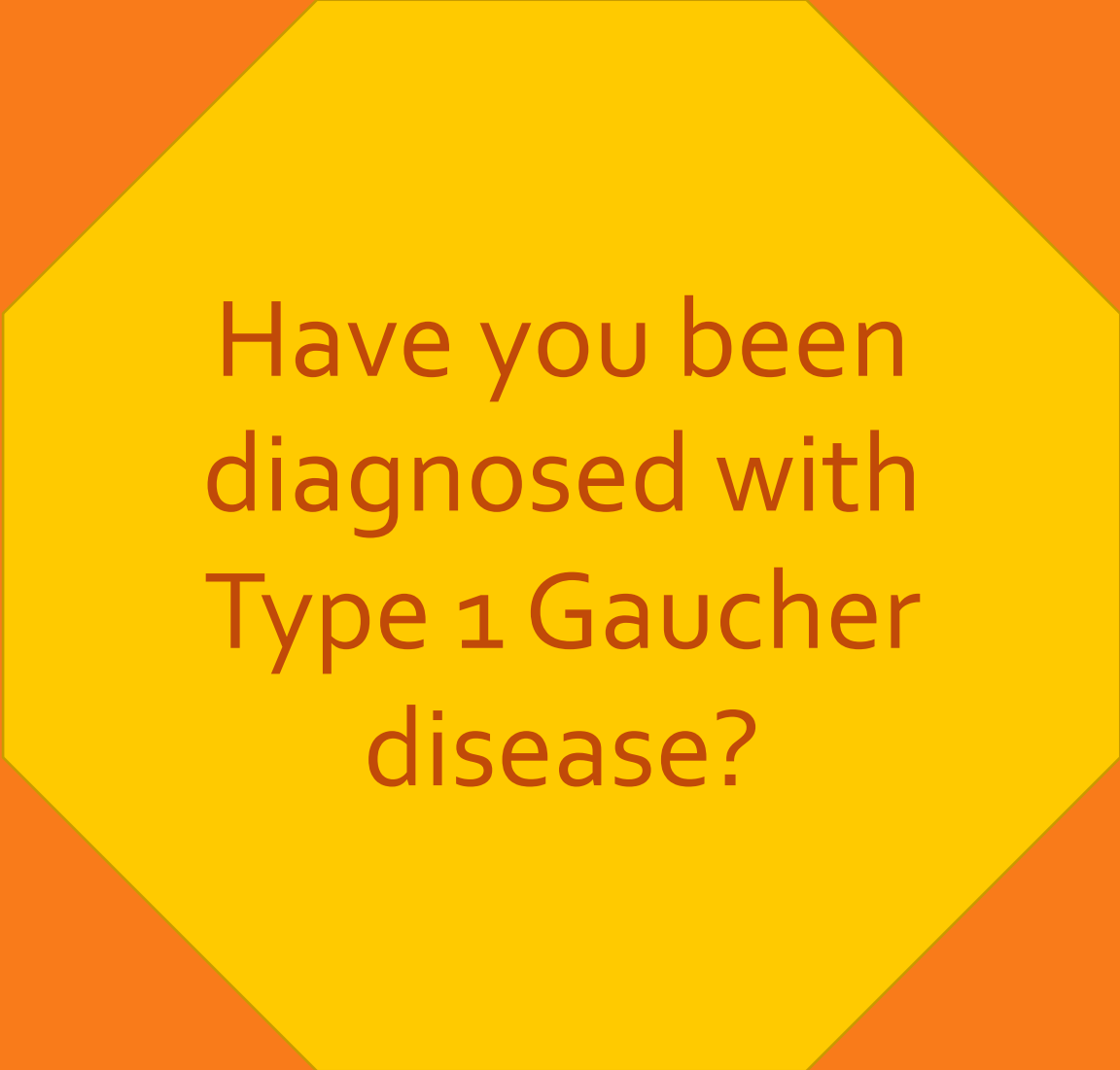


ISMMS n=76

Residence

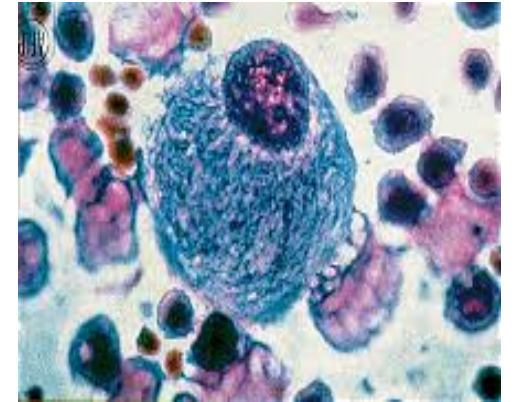


NGF n=49

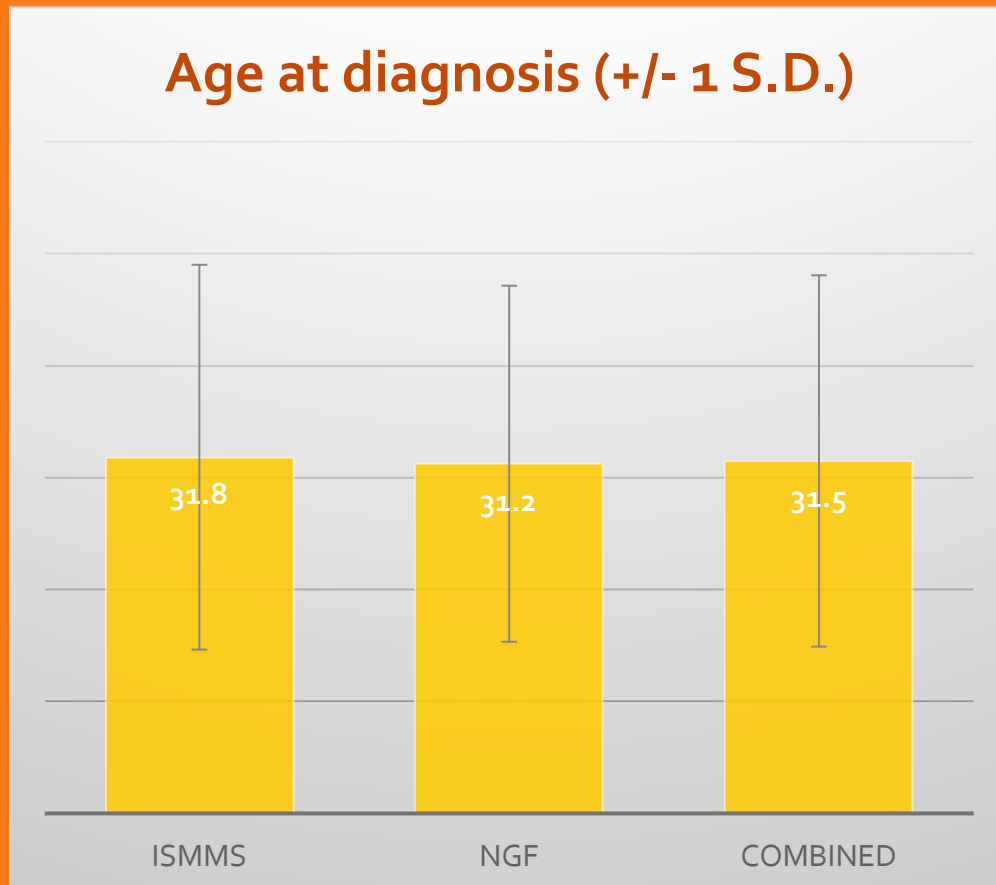


Have you been
diagnosed with
Type 1 Gaucher
disease?

GAUCHER DETAILS

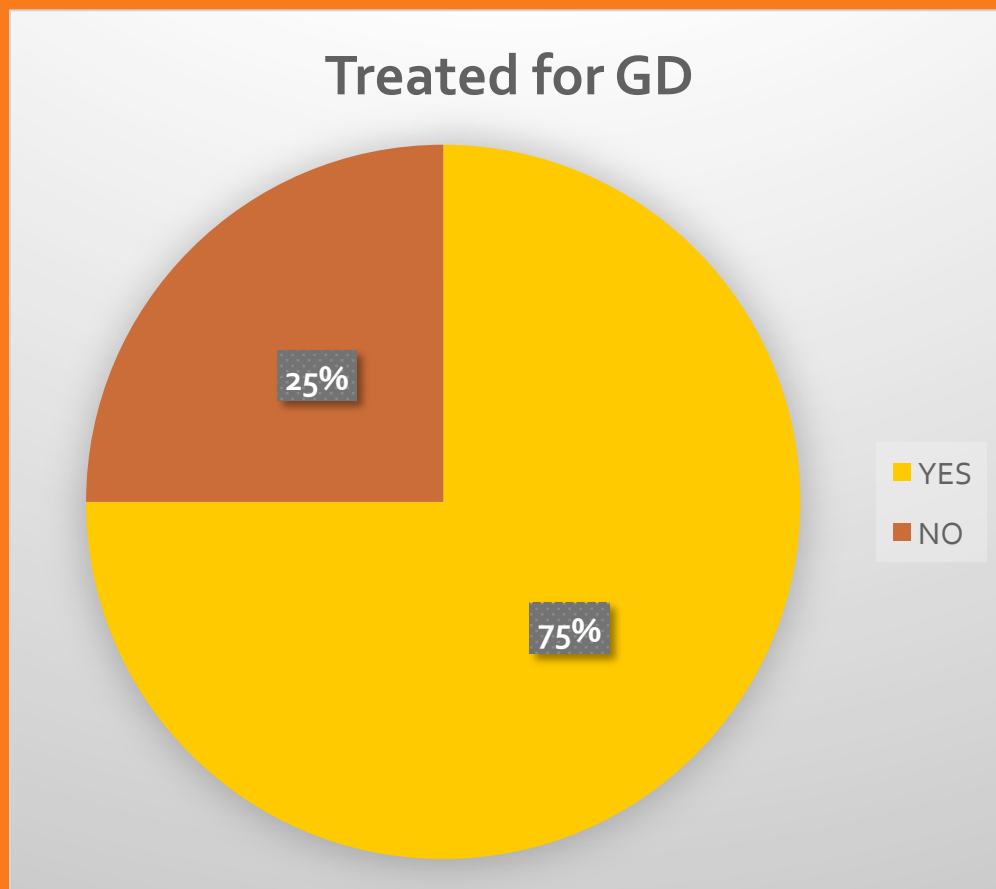


The average Mount Sinai participant was diagnosed at 31.8 years of age, while the average NGF participant was diagnosed at 31.2 years of age

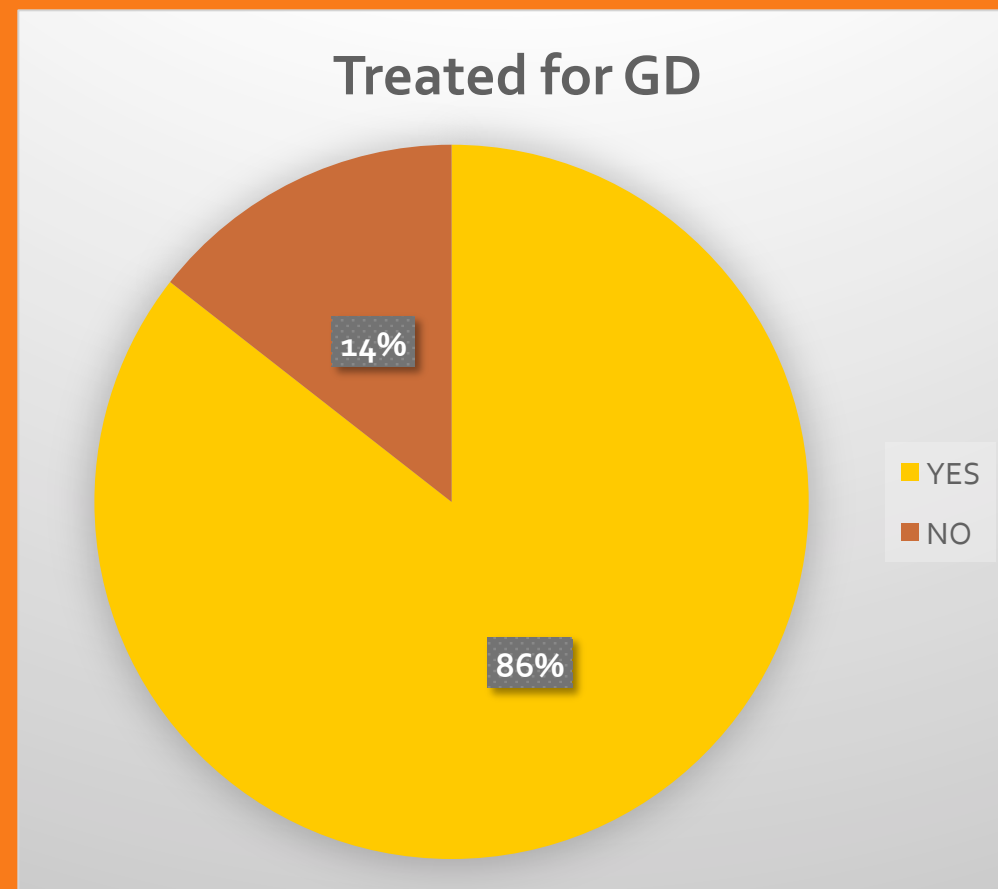


- ISMMS n=76
 - Average age at diagnosis=31.8 years
 - Standard deviation=17.2 years
- NGF n=49
 - Average age at diagnosis=31.2 years
 - Standard deviation=15.9 years
- Combined n=125
 - Average age at diagnosis=31.5 years
 - Standard deviation=16.6 years

Overall, approximately 80% of participants receive treatment for Gaucher disease



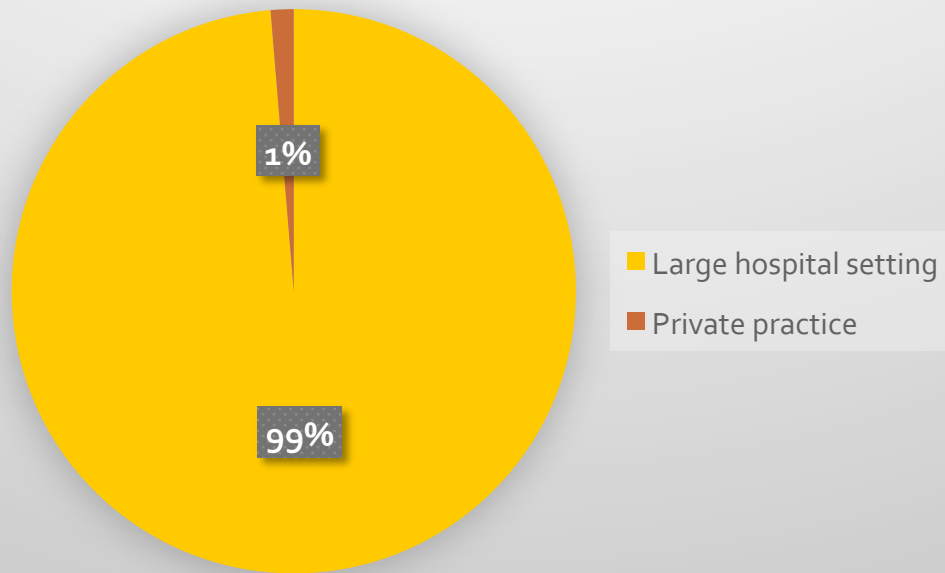
ISMMS n=76



NGF n=49

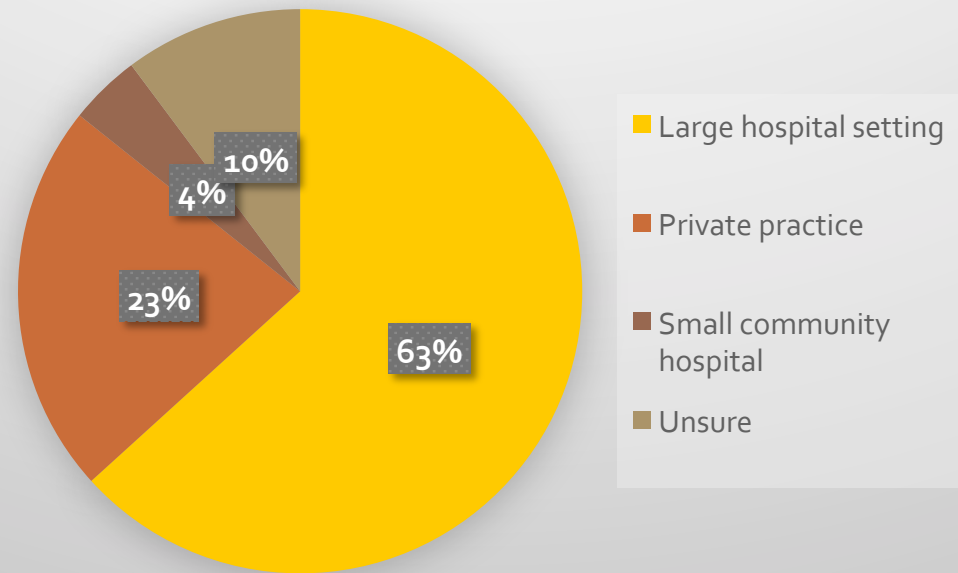
Most participants (approximately 85%) are followed for Gaucher disease in a large hospital setting

In what type of medical practice are you followed for Gaucher disease?



ISMMS n=76

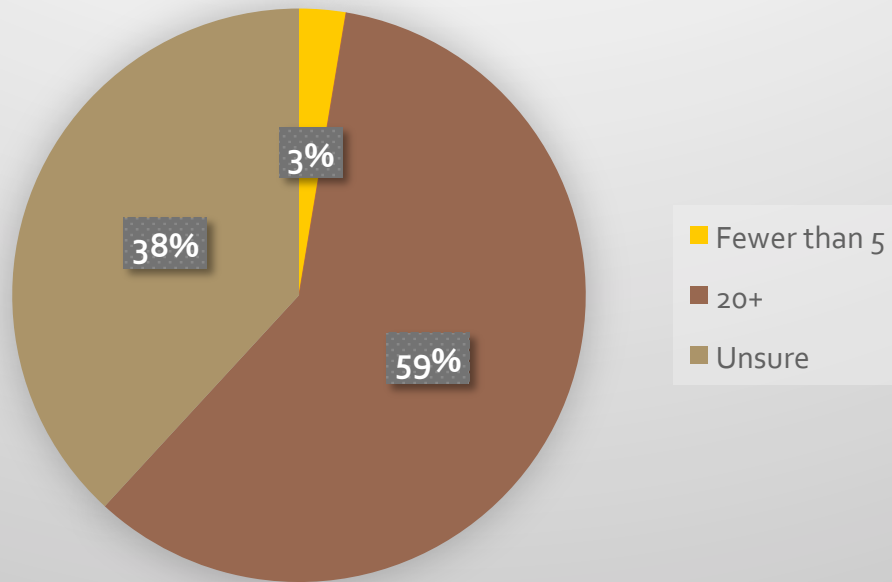
In what type of medical practice are you followed for Gaucher disease?



NGF n=49

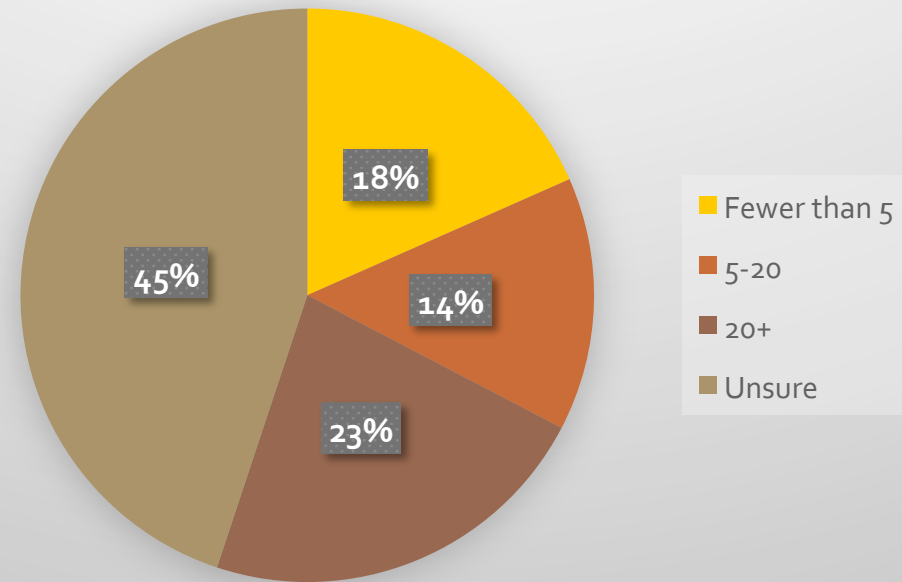
Approximately 41% were unsure how many GD patients their doctor follows, and 45% answered that their doctor follows 20+ patients

How many patients with Gaucher disease does your doctor follow?



ISMMS n=76

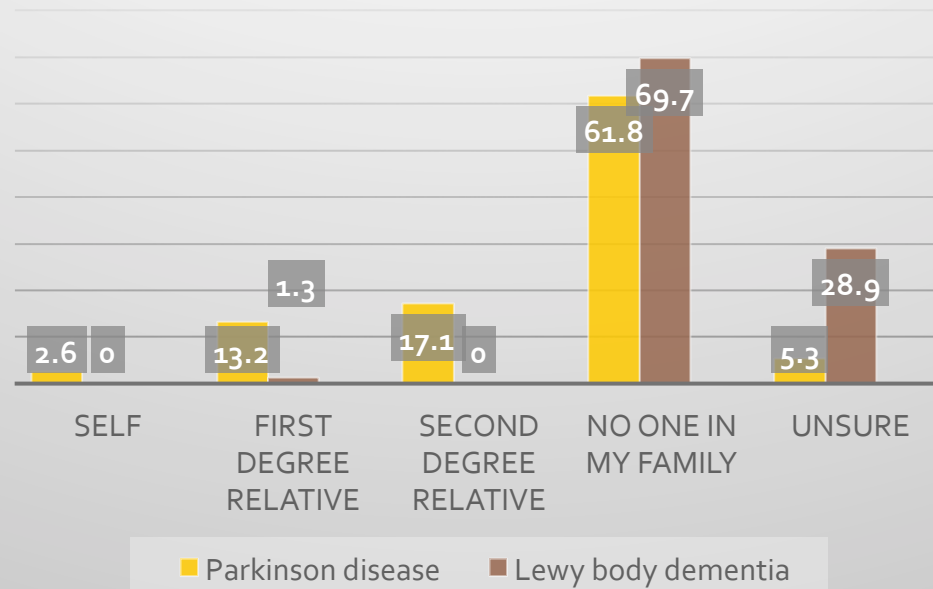
How many patients with Gaucher disease does your doctor follow?



NGF n=49

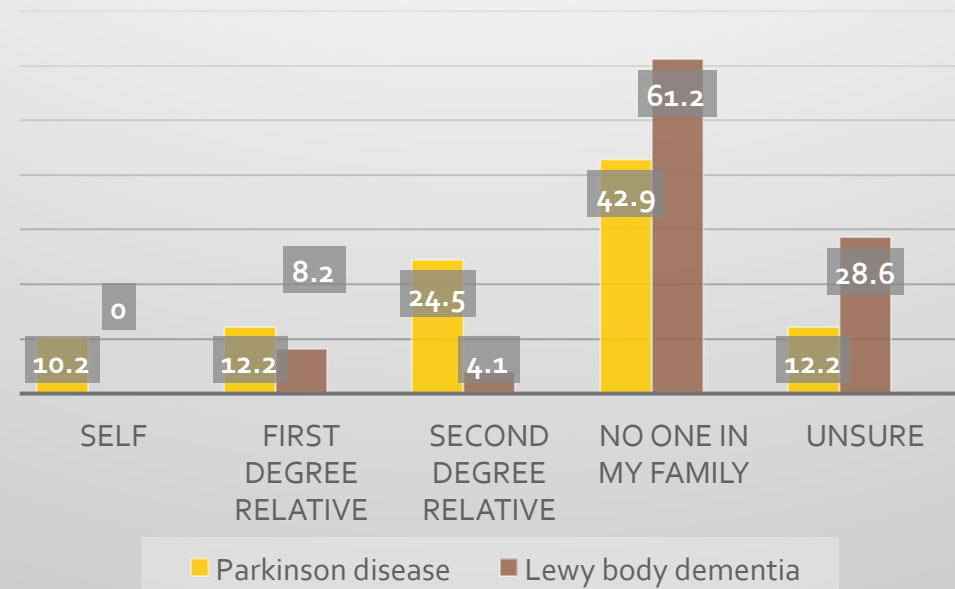
Overall, 54% of participants reported that no one in their family has PD, and 66% reported that no one in their family has LBD

As far as you are aware, do you or anyone in your family have PD or LBD?



ISMMS n=76

As far as you are aware, do you or anyone in your family have PD or LBD?

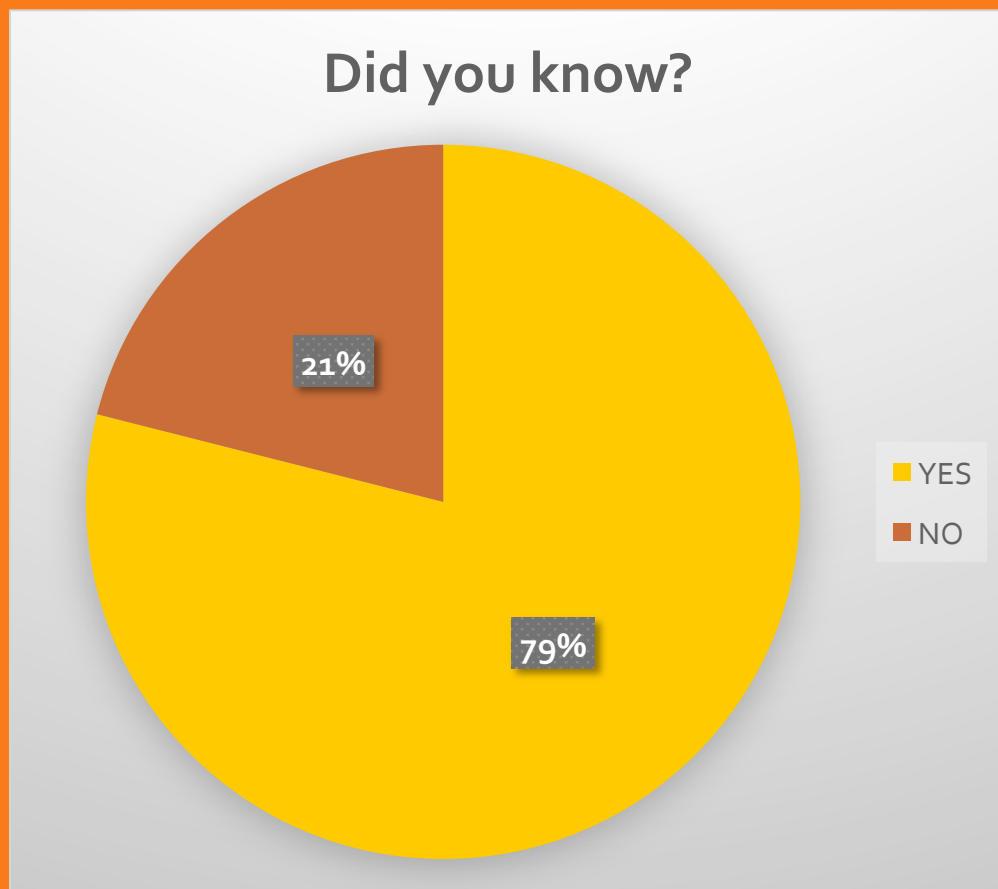


NGF n=49

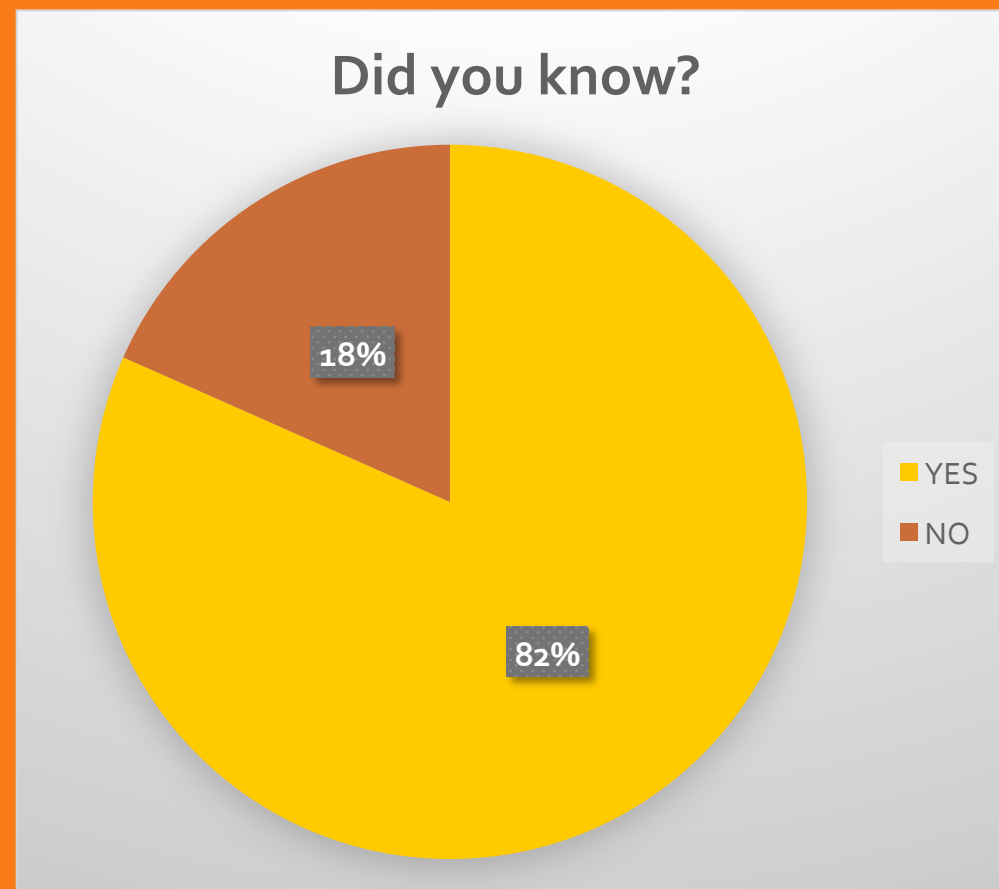
THE MONEY SHOT



Prior to taking this survey, were you aware that people with Gaucher disease have a higher risk of developing Parkinson disease than the general population?



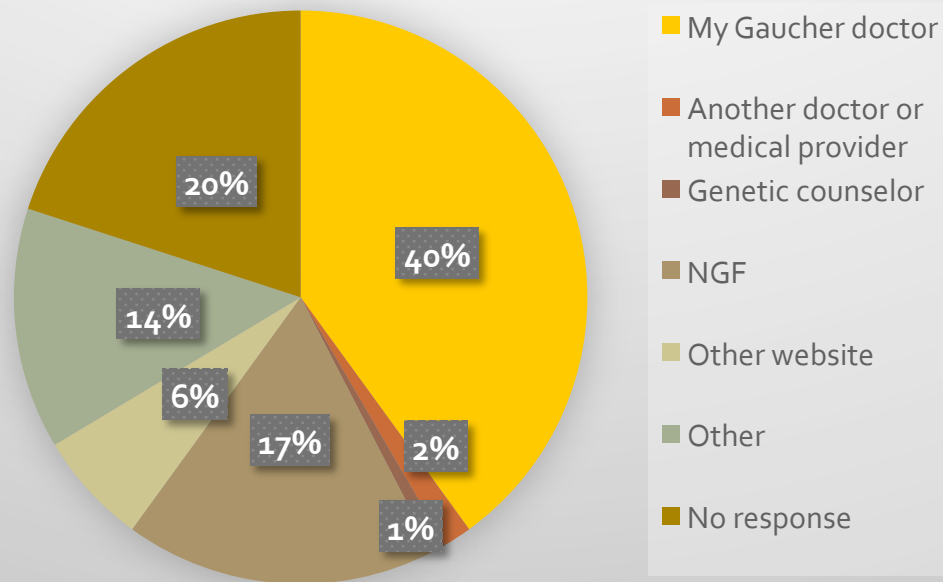
ISMMS n=76



NGF n=49

Participants were loyal to their recruitment site and one participant answered that they first learned from a genetic counselor

How did you first learn about the increased risk of developing Parkinson disease?

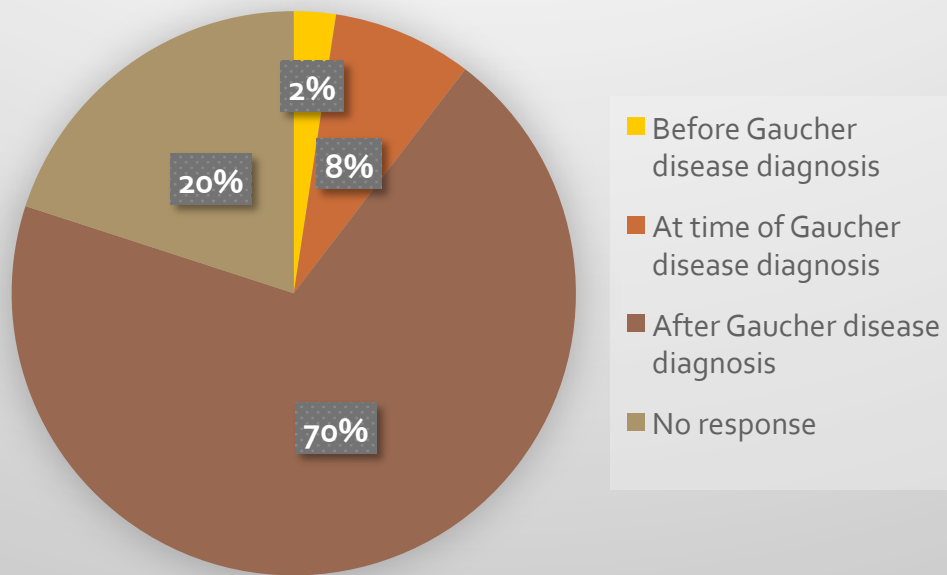


Combined n=125

- Other
 - "Doing research over the years since my diagnosis in 1968"
 - "Gaucher patient meetings"
 - "Research, internet, NIH study"
 - "Symptoms"
 - "My own reading"
 - "I do not remember"

Most participants reported first learning of the increased risk sometime after diagnosis, rather than at the time of diagnosis

When were you first informed of the increased risk of developing Parkinson disease?

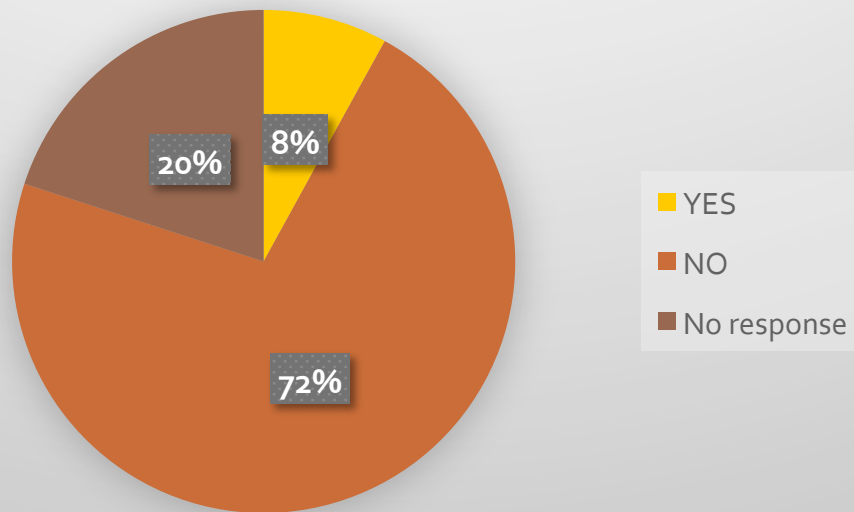


Combined n=125

- Who first learn of the increased risk at the time of Gaucher disease diagnosis?
 - ISMMS participants: ~13%
 - NGF participants: 0%

Most participants answered that they have not made changes based on knowledge of the risk, indicating that it is not a source of significant stress

Have you ever made any medical or lifestyle changes based on knowledge of this risk?

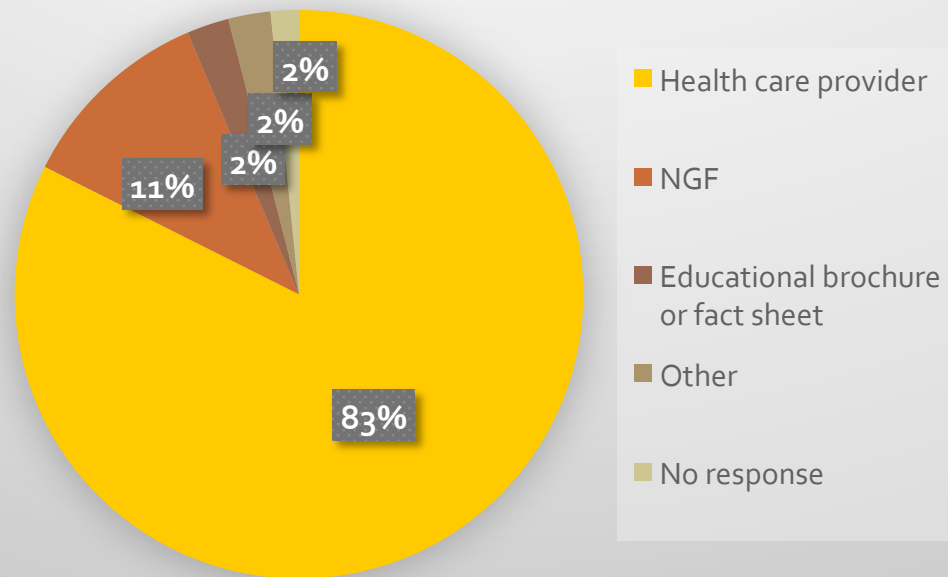


Combined n=125

- If yes, what changes are you making?
 - "Exercise more"
 - "Take vitamin D"
 - "Yearly exams"

A majority of participants believe the best way to find out about the increased risk is from a health care provider

The ideal way to find out about the increased Parkinson disease risk is from:

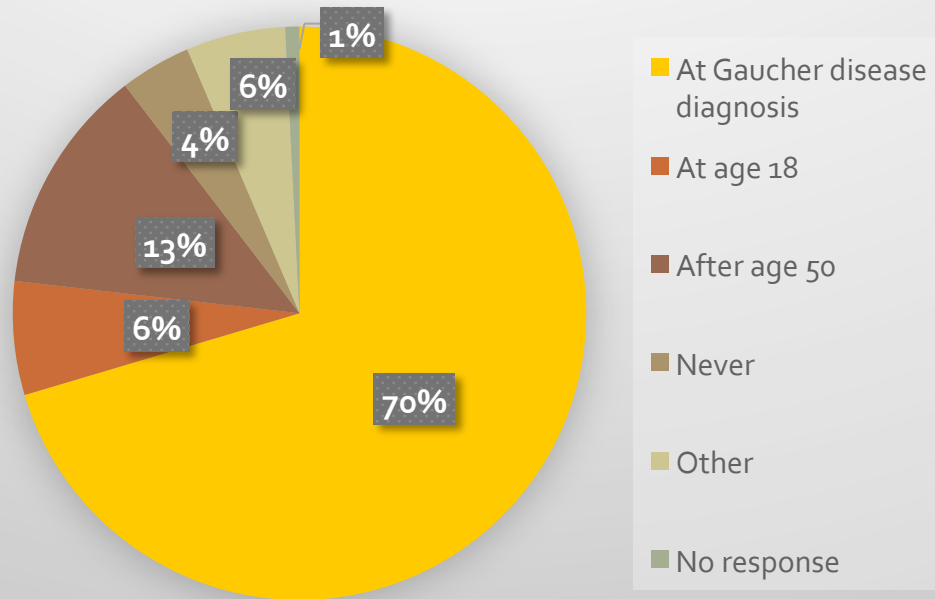


Combined n=125

- If other, what do you think is the ideal way to find out?
 - "Parkinson foundation"
 - "All of above and read everything you can find"

Most participants believe the best time to find out about the increased risk is at the time of Gaucher disease diagnosis

The ideal time to find out about the increased Parkinson disease risk is:

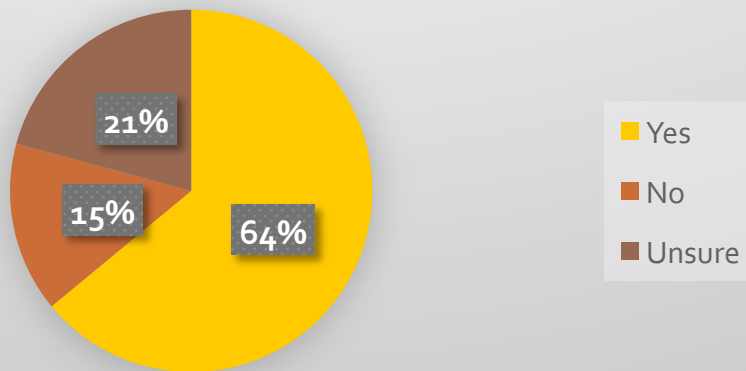


Combined n=125

- If other, when do you think the ideal time is to find out?
 - "No good time, but should be told no later than when symptoms of Parkinson's may be evident"
 - "When something can be done or when it manifests"
 - "As soon as possible"
 - "Right now"

Only 15% of participants indicated they would not be interested in an online exam to evaluate for symptoms of Parkinson disease

If there were a study offering an online physical examination performed by a neurologist to evaluate for symptoms of Parkinson, would you be interested in participating?



Combined n=125

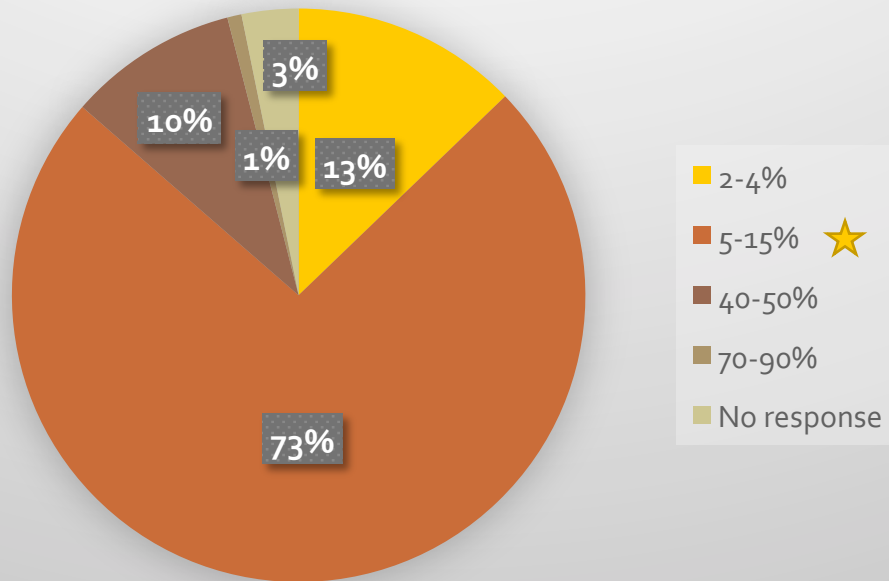
- Future direction for a study?

KNOWLEDGE



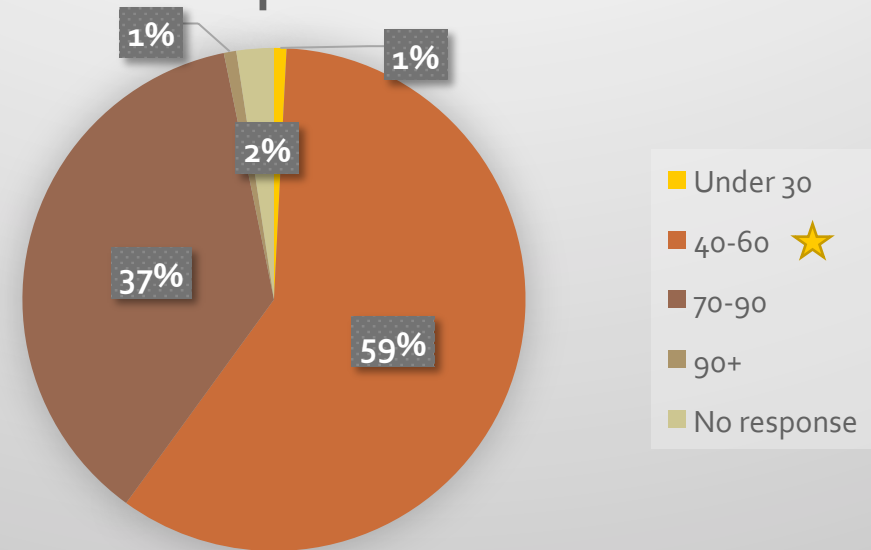
73% of participants correctly answered the risk of developing Parkinson disease, while 59% correctly answered the average age that symptoms present

The risk for Parkinson disease in patients with Gaucher disease is approximately:



Combined n=125

The average age that symptoms of Parkinson disease start in Gaucher patients is:

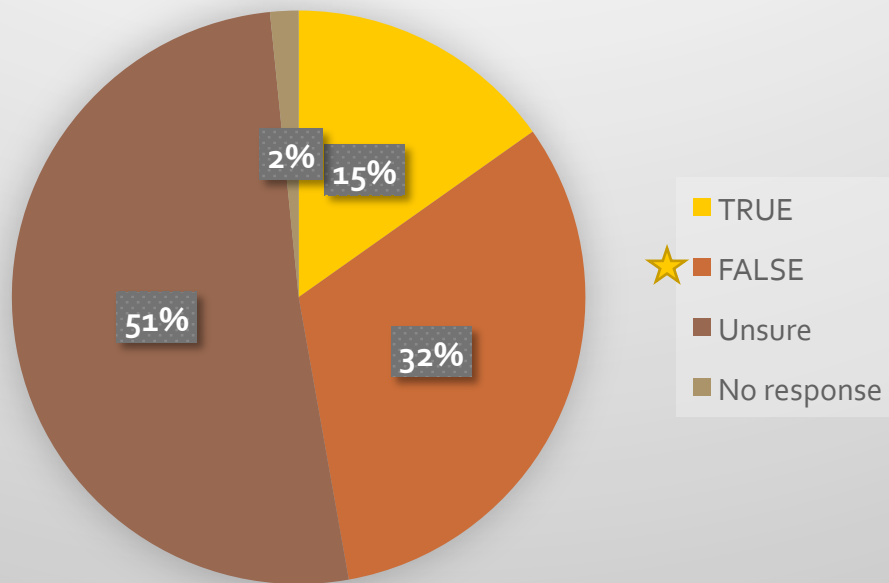


Combined n=125

★ Correct answer

Approximately half were unsure if Gaucher treatment reduces Parkinson risk, reflecting the uncertainty in the scientific community

Treatment for Gaucher disease will reduce the risk of developing Parkinson disease

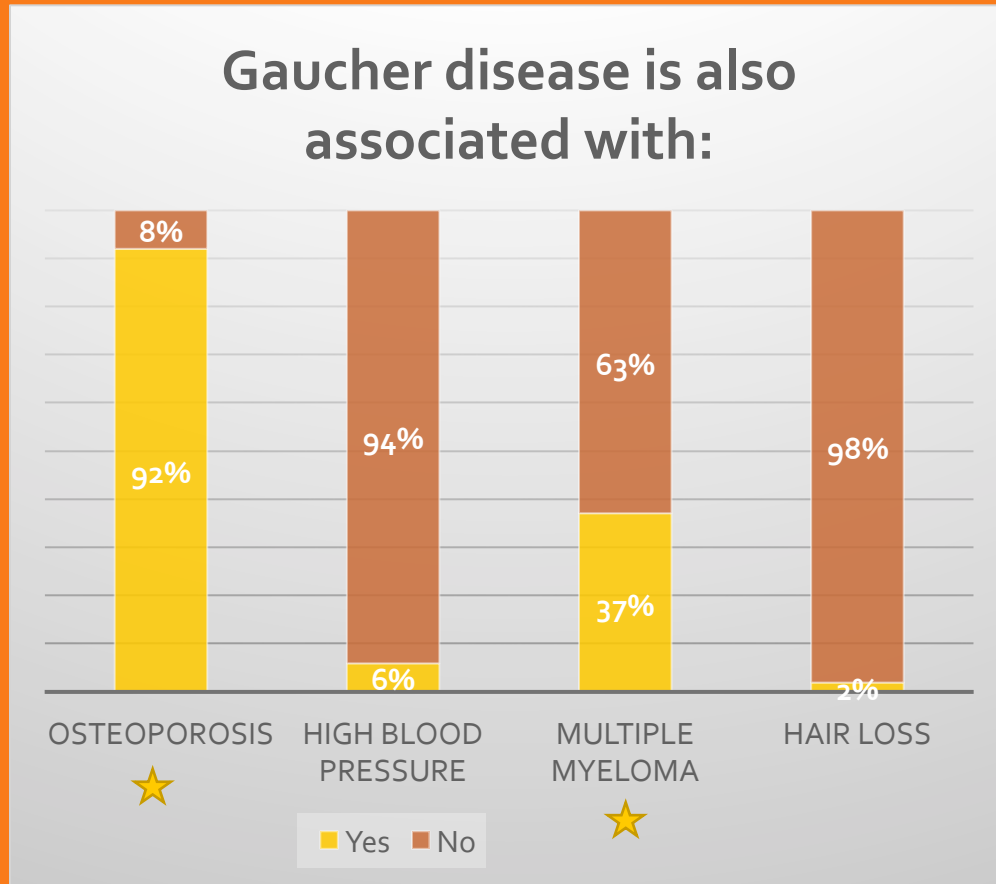


Combined n=125

★ Correct answer

- “To date, enzyme replacement treatment used to treat Gaucher disease does not appear to benefit individuals with GBA mutations who develop Parkinson disease.” – Cook and Schulze 2017
- “Evidence from a variety of in vitro and in vivo models indicate that GCase activity and α -synuclein levels have a reciprocal relationship, although the molecular mechanisms underlying this are not fully understood.” – Balestrino and Schapira 2018

A vast majority of participants knew of the association with osteoporosis, but only 37% knew of the association with multiple myeloma



Combined n=125

★ Correct answer

- “Data emerging from the International Collaborative Gaucher Group (ICGG) Gaucher Registry together with other contemporary clinical surveys have revealed a close association between Gaucher disease and non-Hodgkin's B-cell lymphoma and myeloma and Gaucher disease and Parkinson's disease.” –Cox et al. 2015

CONCLUSION



Patients wish to find out about the increased Parkinson risk from their health care provider at the time of Gaucher diagnosis

- Health care providers should counsel Gaucher patients about the increased Parkinson disease risk
 - This should include the risk number as well as the average age at onset
- Information about the risk should be reiterated at every visit
 - The study participants were well educated and well informed, yet 20% reported not previously knowing about the increased risk of Parkinson disease
- Information about comorbidities should be reiterated at every visit
 - Only 37% of participants knew about the increased risk of multiple myeloma
 - But what about timing? Risk for multiple myeloma is 50-60s

Study limitations include sample size and sample characteristics

- Sample may not be representative of Gaucher patients elsewhere in the country
- Survey taken by “captive audience” (ISMMS) and those who are interested in and familiar with Gaucher disease (NGF)
- No statistically significant results
 - Prior knowledge of Parkinson disease risk was not predictive of answering the knowledge-based questions correctly (CI spanned 1)

Future directions include addressing the limitations and creating new studies

- Survey a larger cohort to include other demographics, including participants from areas where there are few Gaucher patients and doctors
- Assess health care providers' counseling practices with regard to increased Parkinson disease risk
- Create a study assessing for symptoms of Parkinson disease
- What about Gaucher disease carriers?

THANK YOU!!

- Manisha Balwani, MD
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- Samantha Rubinstein, VP of Education, Awareness and Patient Advocacy at NGF
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- Attending physicians
- Residents and fellows





