

# Results of a survey of NF1 patients- defining the symptom burden of cutaneous neurofibromas

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Cutaneous Neurofibroma Working Group

Ashley Cannon, PhD, MS, CGC

Dominique Pichard, MD

Gregg Erickson, Patient Representative



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION







“Paradigms are powerful because they create the lens through which we see the world... if you want small changes in your life, work on your attitude. But if you want big and primary changes, work on your paradigm”

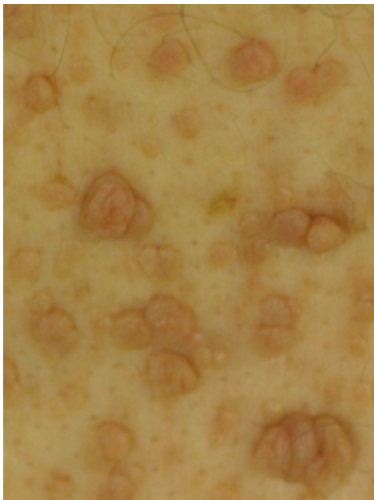
- Dr. Stephen R. Covey





# cNF background

- cNFs affect more than 99% of adults with NF1
- No malignant potential but have significant negative effects on quality of life
- Current treatment is limited, treat a subset of cNFs, and can result in scarring and future tumor recurrence
- Development of effective medical therapies is needed



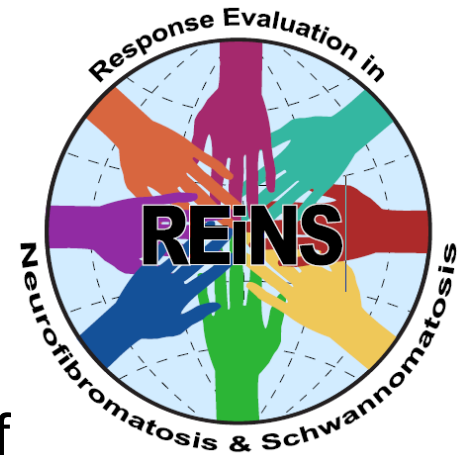
# Patient-centered cNF research

- Lack of data concerning how patients assess morbidity related to cNFs and how they view current and potential cNF treatments
- As therapies become available for cNFs, it is critical to understand the patient perspective to guide the design of clinical trials
- Federal funding and regulatory organizations (e.g. FDA, PCORI) are strongly encouraging the involvement of patient representatives to facilitate better informed decisions for patient-centered research



# Adult cNF survey

- Created by the REiNS Cutaneous Neurofibroma Working Group
  - Reviewed and piloted by REiNS patient representatives
  - FDA provided feedback (Melissa Reyes, MD)
- Designed to collect basic demographic information, details about the patient's cNFs, views on morbidity related to specific aspects of cNFs, and views regarding current and potential future cNF treatment
- A survey link was distributed via the Children's Tumor Foundation Patient Registry email blast
- Inclusion criteria: NF1, at least 1 cNF, at least 18 years old, and English speaking



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[www.nfregistry.org](http://www.nfregistry.org)

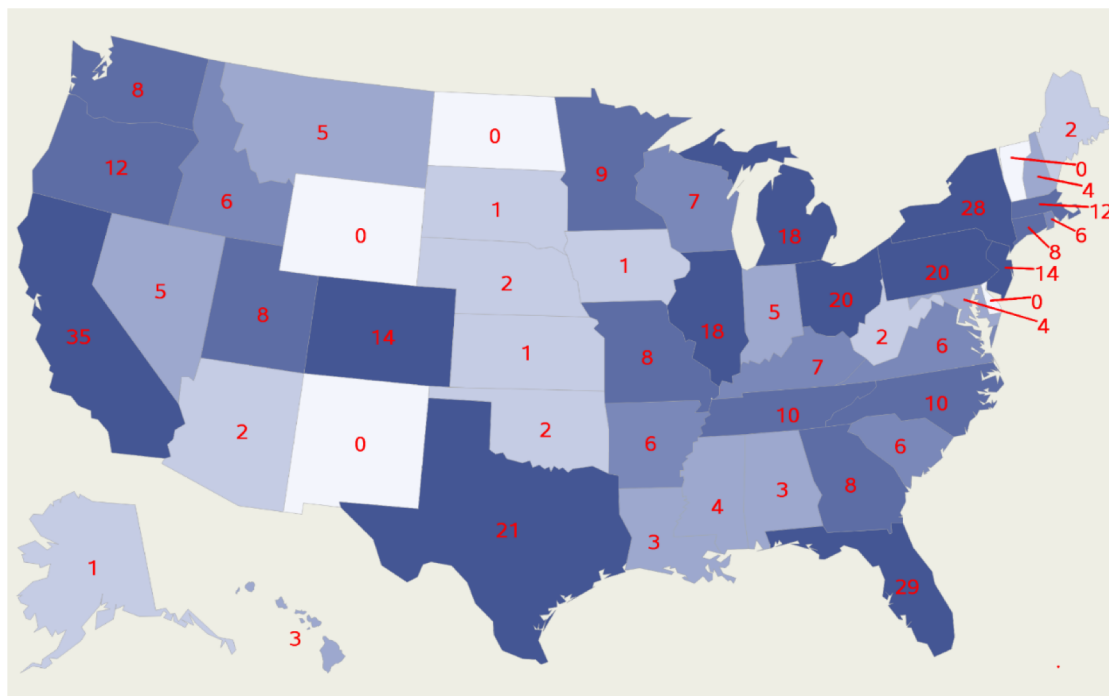
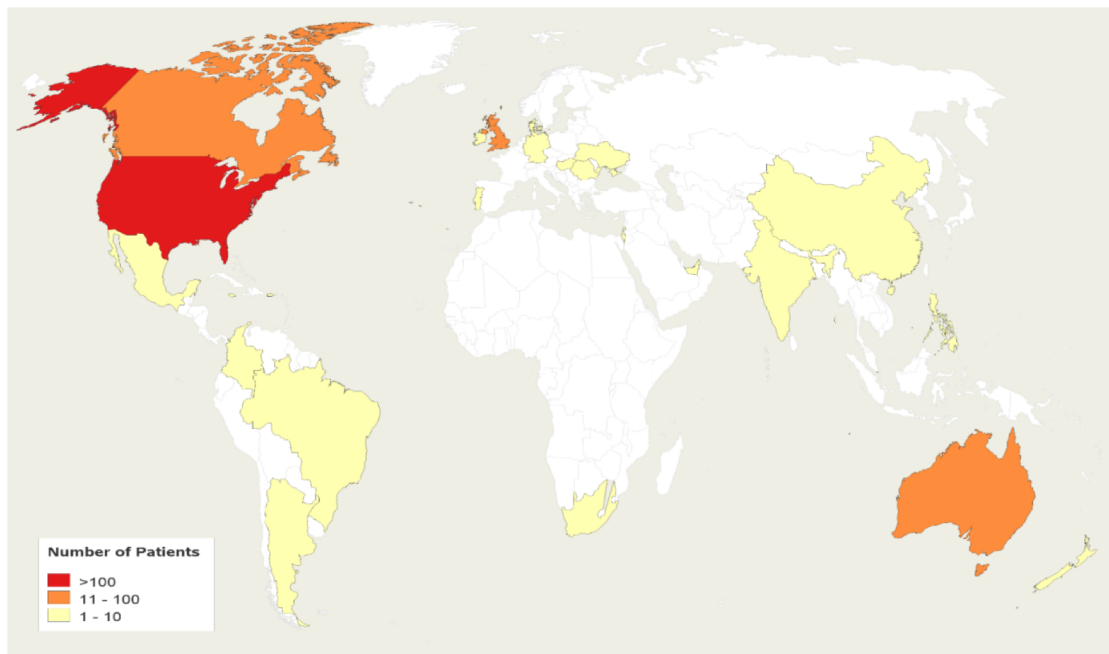




<b>Characteristics (n=548)</b>	<b>Mean (SD) or N (%)</b>
Age	44.9 (±13.7)
Sex	
Female	385 (67.7%)
Male	171 (30.1%)
Other	1 (0.2%)
Not answered	12 (2.1%)
Race	
American Indian or Alaska Native	7 (1.2%)
Asian	20 (3.5%)
Black of African American	15 (2.6%)
Native Hawaiian or Other Pacific Islander	5 (0.9%)
White	488 (85.8%)
Other	20 (3.5%)
Not answered	14 (2.5%)
Ethnicity	
Hispanic or Latino	36 (6.3%)
Not Hispanic or Latino	413 (72.6%)
Other	91 (16.0%)
Not answered	29 (5.1%)
Education	
Did not complete high school	21 (3.7%)
High school degree or equivalent (e.g. GED)	95 (16.7%)
Some college but no degree	131 (23.0%)
Associate degree (2 year college degree)	83 (14.6%)
Bachelor degree (4 year college degree)	145 (25.5%)
Graduate degree	80 (14.1%)
Not answered	14 (2.5%)
Work outside of home	
Yes	343 (60.3%)
No	213 (37.4%)
Not answered	13 (2.3%)
First person in family with NF	
Yes	368 (64.7%)
No	188 (33.0%)
Not answered	13 (2.3%)

14.6% response rate



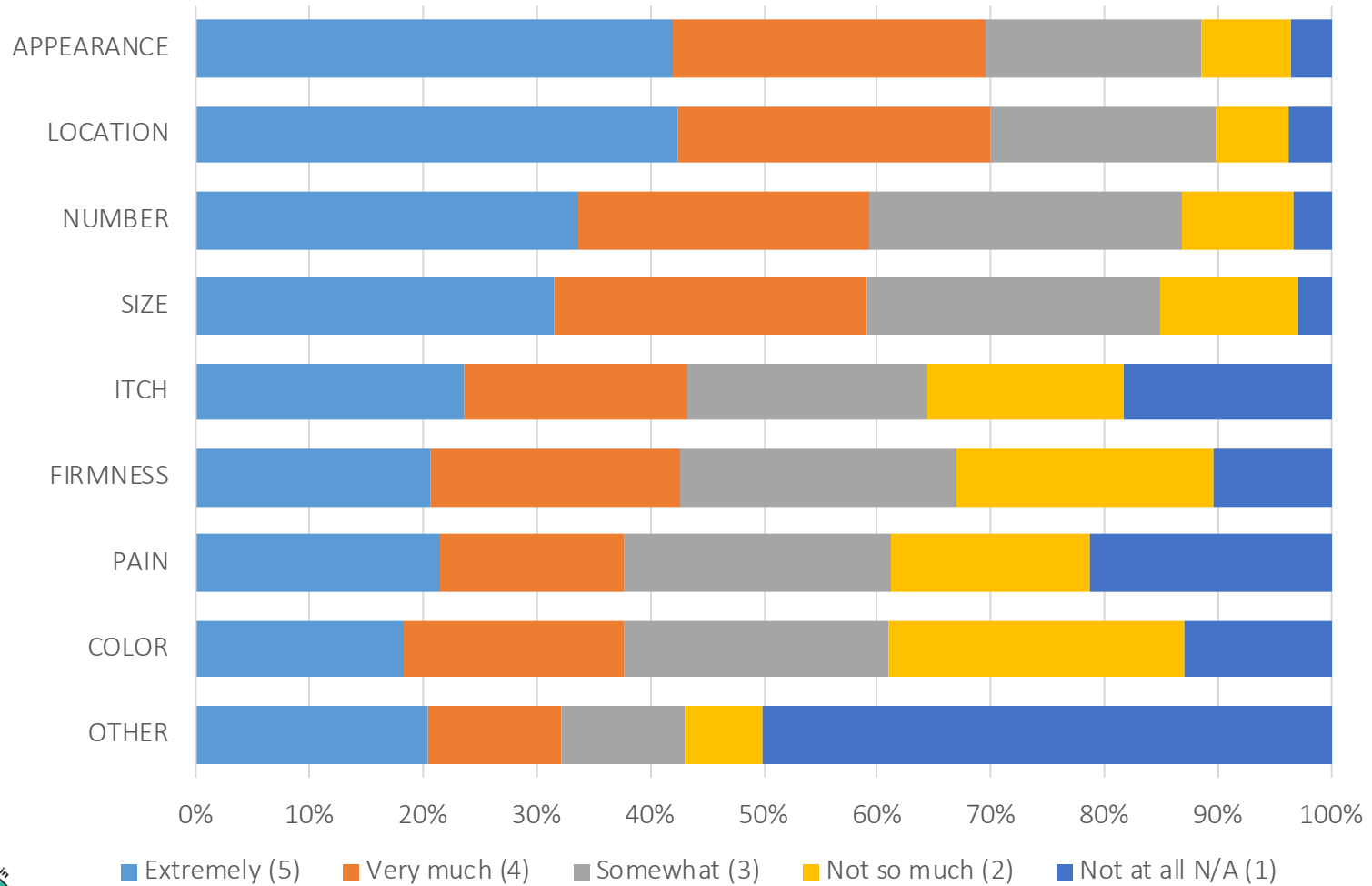


<b>Respondent cNF Characteristics</b>	<b>N (%)</b>
<b>Number of cNFs</b>	
Not Answered	39 (6.9%)
1-19 over entire body	89 (15.6%)
20-99 over entire body	136 (23.9%)
100-500 over entire body	185 (32.5%)
> 500 over entire body	122 (21.1%)
<b>Age at first cNF</b>	
Not Answered	41 (7.2%)
Less than 10 years old	147 (25.8%)
10-19 years old	239 (42.0%)
20-29 years old	104 (18.3%)
30-39 years old	30 (5.3%)
40 years or older	8 (1.4%)
<b>Body locations with cNFs</b>	
Scalp	289 (50.8%)
Face	375 (65.9%)
Neck	364 (64.0%)
Trunk (chest, belly, back)	494 (86.8%)
Arms	451 (79.3%)
Hands	334 (58.7%)
Legs	364 (64.0%)
Feet	301 (52.9%)
Genitals	222 (39.0%)
Nipple/Areola	300 (52.7%)
Other	39 (6.9%)
<b>Flat cNF</b>	
Yes	318 (55.9%)
No	86 (15.1%)
I don't know	130 (22.9%)
Not Answered	35 (6.2%)





How much does each FEATURE of your **raised** cutaneous neurofibromas bother you (physically, cosmetically, or emotionally)?

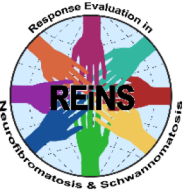
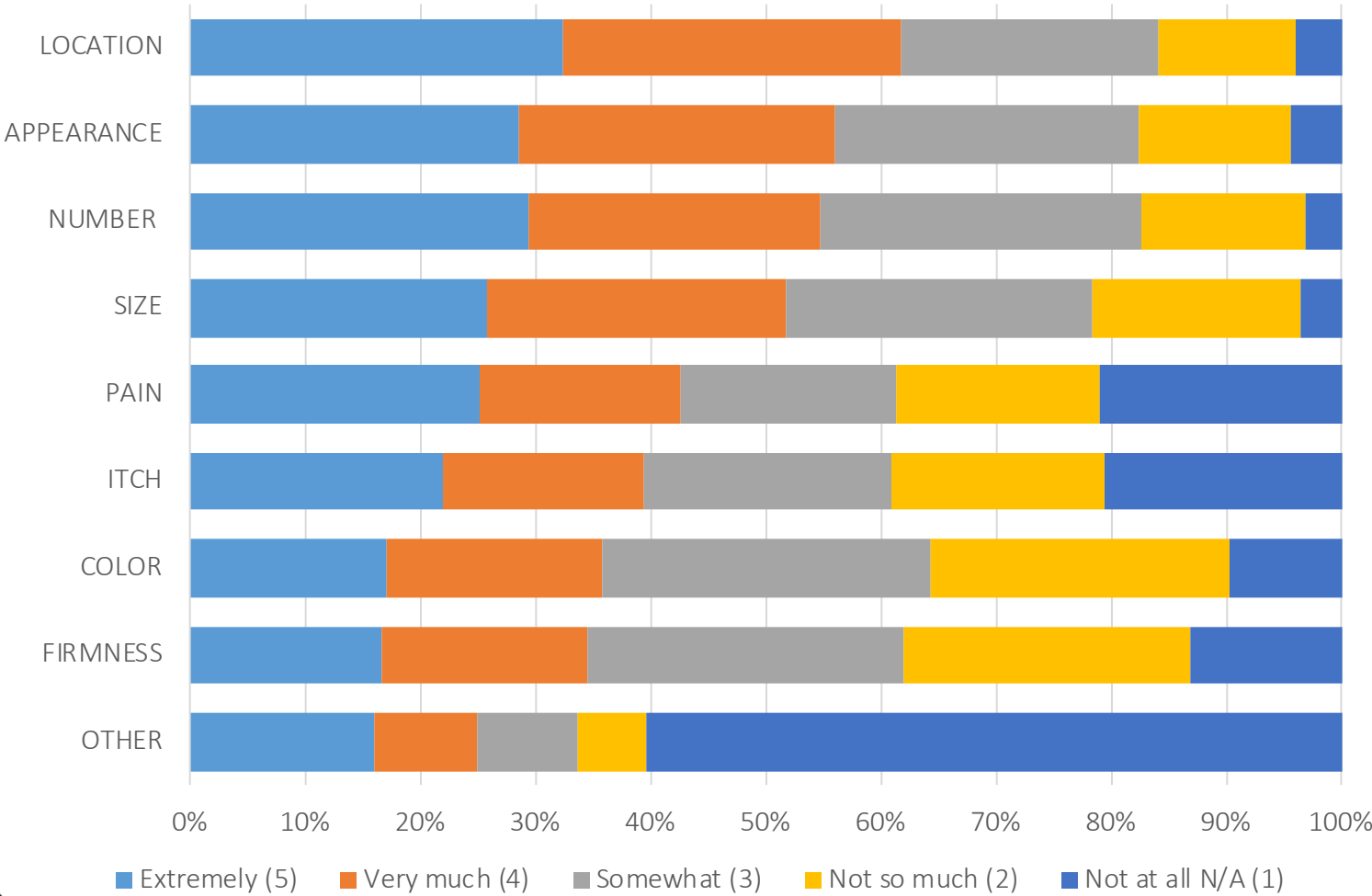


# What is it about the cNF feature(s) that bother you?

- “While the total number can usually be covered by clothing, this can sometimes be restrictive and uncomfortable, especially in hot weather. The location of some of the cutaneous growths is such that they cause bulges underneath clothing that can be difficult to mask or camouflage.”
- “Each time I look in the mirror I see a person who I don't want to be because of the neurofibromas. Inside I see myself as a butterfly however, my appearance may say other wise. I try to have a conversation with a person, however, I see their eyes staring at my lumps and bumps.”
- “While pain is always present I don't have to talk about that, but people always see the tumors. **I can hide my pain, I can't hide the quantity of tumors.**”

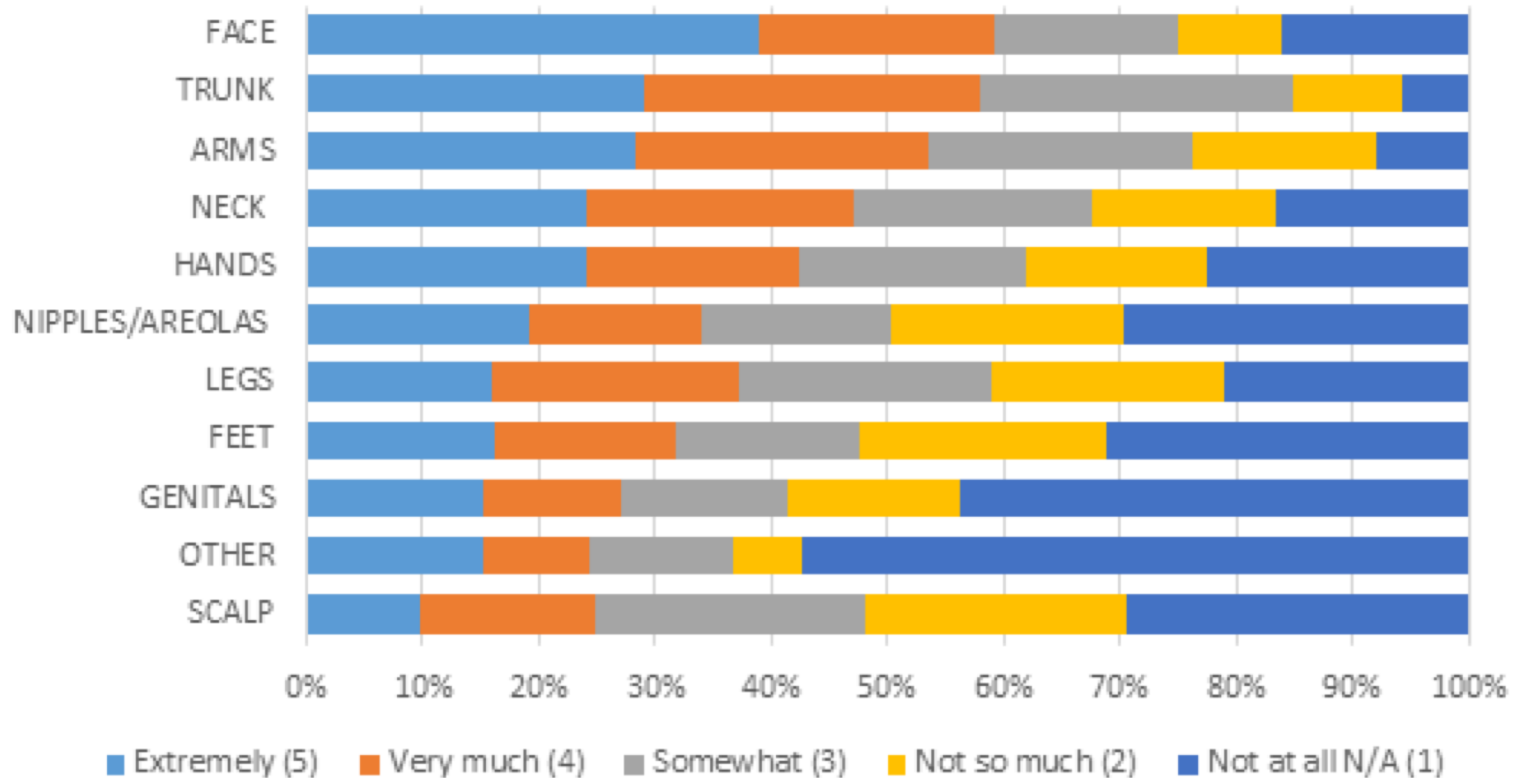


How much does each FEATURE of your flat cutaneous neurofibromas bother you (physically, cosmetically, or emotionally)?





## How much do your cutaneous neurofibromas bother you on each AREA of your body (physically, cosmetically, or emotionally)?



11. When thinking about the raised cutaneous neurofibromas that bother you the most, what is the minimum decrease in cutaneous neurofibroma NUMBER that would be acceptable to you if a new treatment was available? (select one)

a. 0% decrease/No change in number



b. 33% decrease in number



c. 66% decrease in number



d. 100% decrease in number



12. When thinking about the raised cutaneous neurofibromas that bother you the most, what is the minimum decrease in cutaneous neurofibroma SIZE that would be acceptable to you after participating in a treatment trial? (select one)

a. 0% decrease/No change in size



b. 33% decrease in size



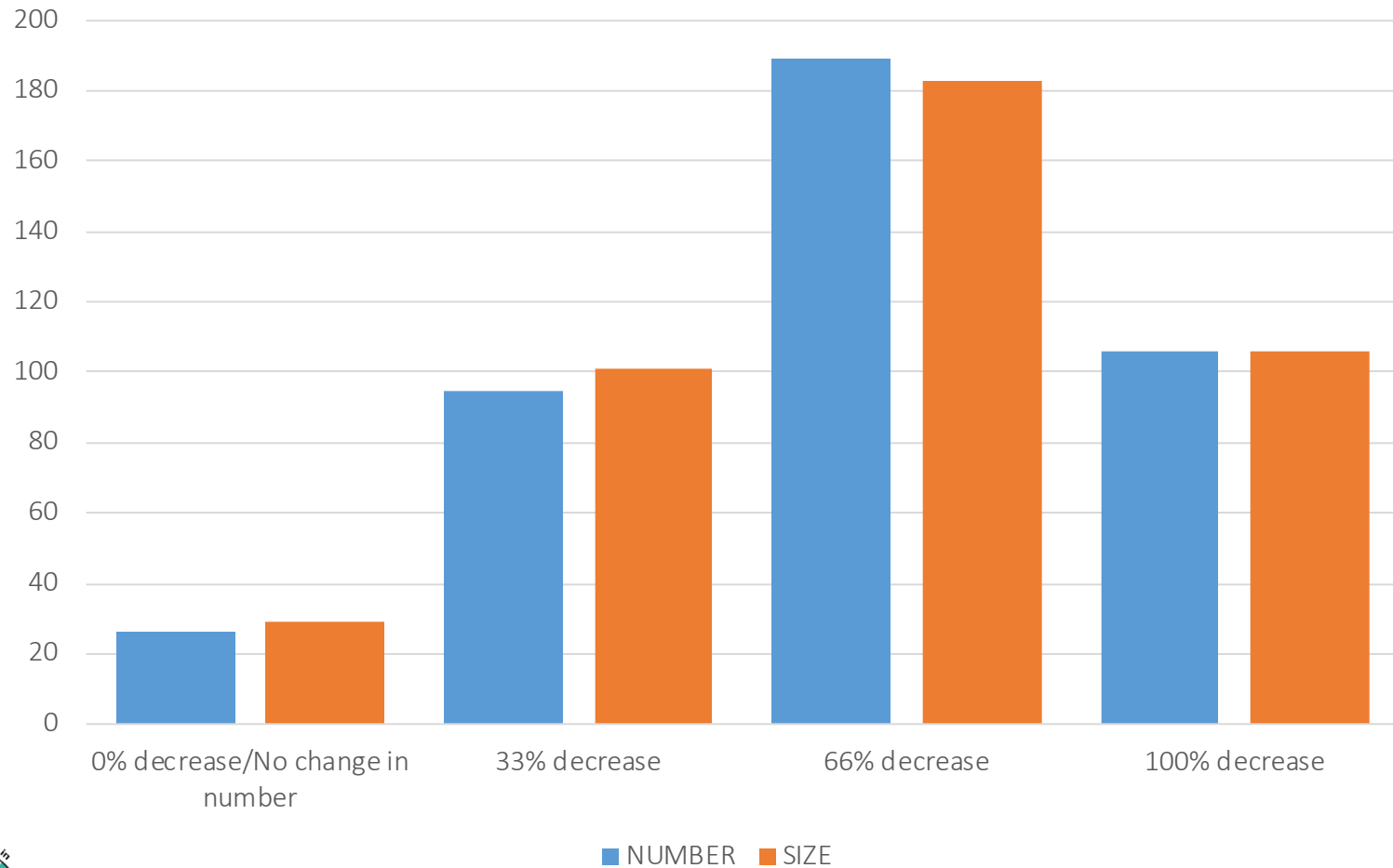
c. 66% decrease in size



d. 100% decrease in size

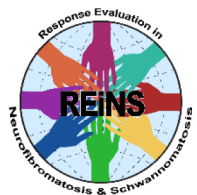


When thinking about the raised cutaneous neurofibromas that bother you the most, what is the minimum decrease that would be acceptable to you after participating in a treatment trial?



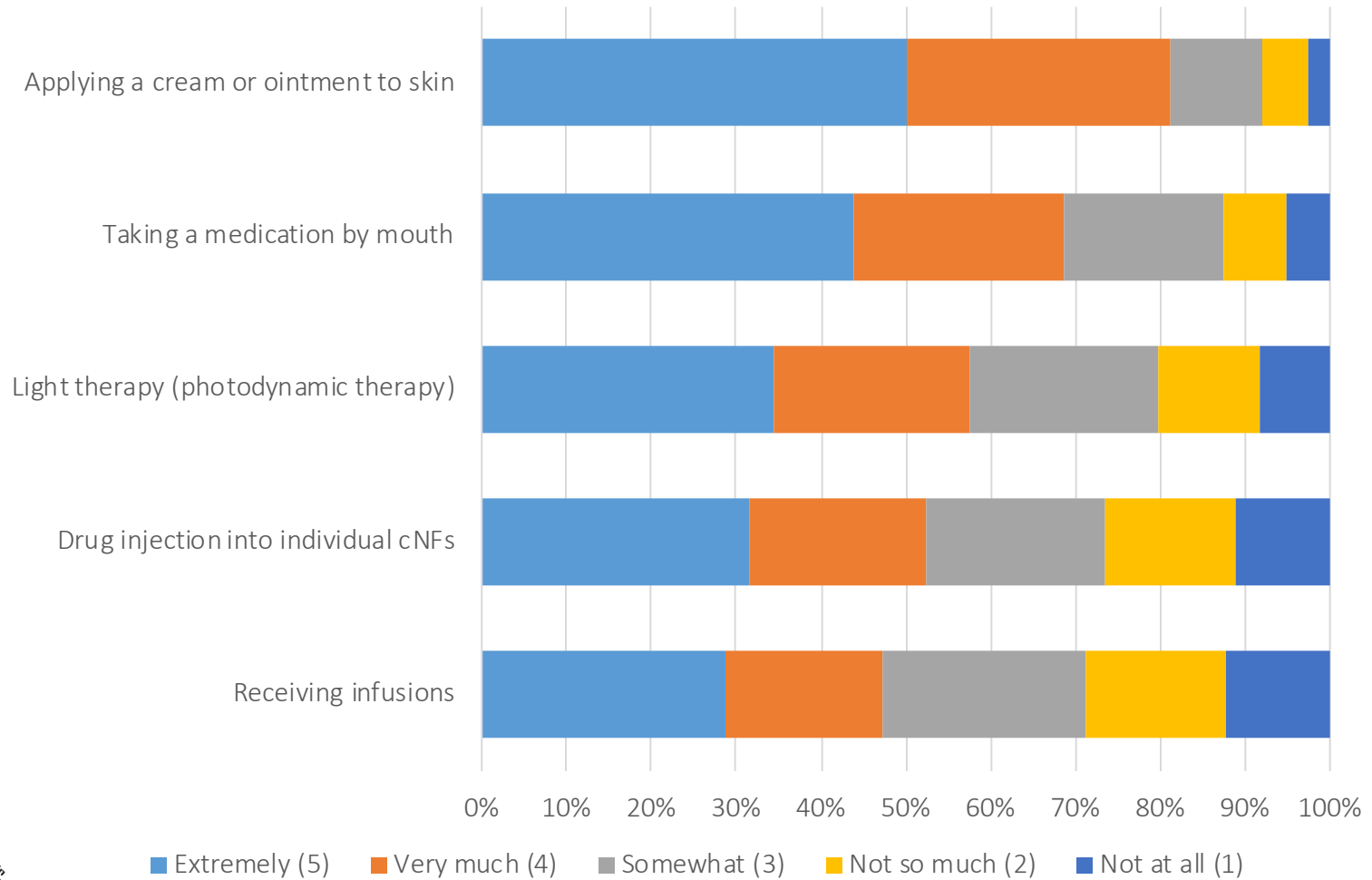
# Current cNF Treatments

	Surgical removal	Laser removal	Radiofrequency ablation	Electrodesiccation
<b>Heard of?</b>				
Not Answered	148 (26.0%)	153 (26.9%)	155 (27.2%)	155 (27.2%)
I don't know	13 (2.3%)	22 (3.9%)	22 (3.9%)	11 (1.9%)
No	55 (9.7%)	177 (31.1%)	320 (56.2%)	212 (37.3%)
Yes	353 (62.0%)	217 (38.1%)	72 (12.6%)	191 (33.6%)
<b>Tried?</b>				
Not Answered	151 (26.5%)	156 (27.4%)	155 (27.2%)	158 (27.8%)
No	147 (25.8%)	375 (65.9%)	402 (70.6%)	366 (64.3%)
Yes	271 (47.6%)	38 (6.7%)	12 (2.1%)	45 (7.9%)
<b>Willing to?</b>				
Not Answered	152 (26.7%)	153 (27.0%)	153 (26.9%)	157 (27.6%)
Maybe	67 (11.8%)	86 (15.1%)	128 (22.5%)	107 (18.8%)
No	17 (3.0%)	10 (1.8%)	13 (2.3%)	22 (3.9%)
Yes	333 (58.5%)	320 (56.2%)	275 (48.3%)	283 (49.7%)





## Assuming equal effectiveness and safety, what is your willingness to try these EXPERIMENTAL treatments for cutaneous neurofibromas?

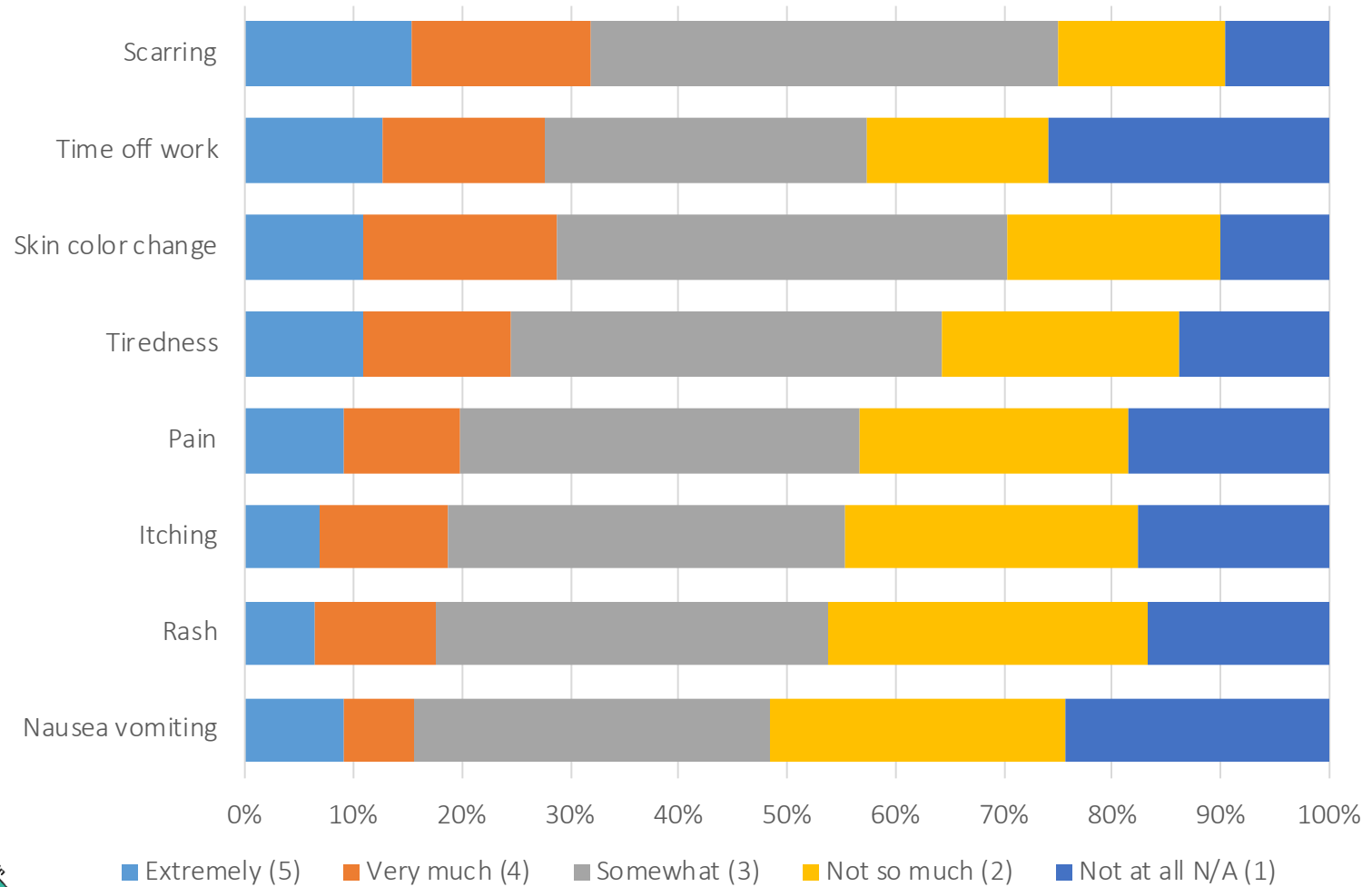


# How long would you be willing to be treated for cutaneous neurofibromas? (select all that apply)

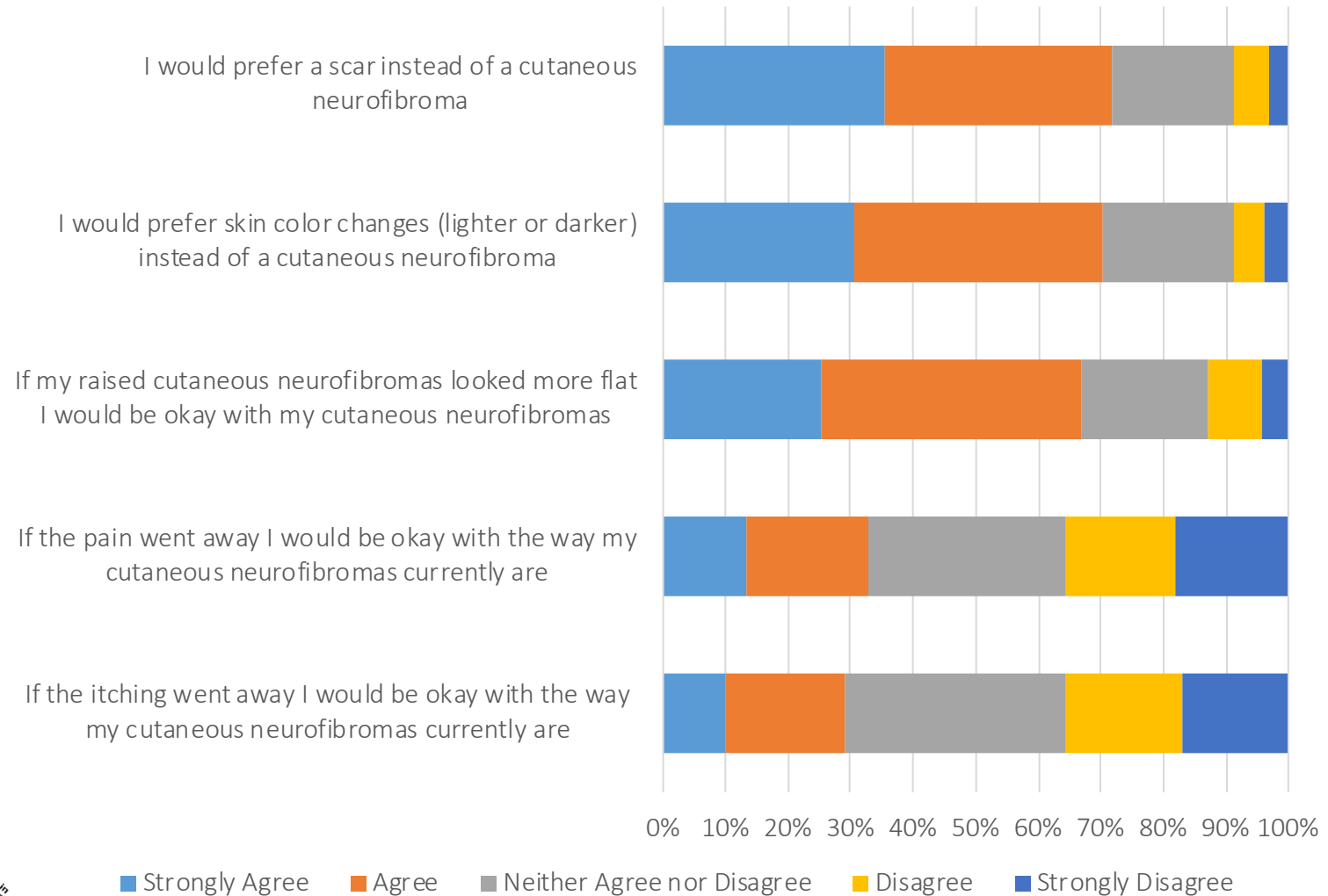
<b>Treatment Frequency</b>	<b>N (%)</b>
One day treatment only	104 (18.3%)
Once a week	170 (29.9%)
Once a month	186 (32.7%)
Once a year	127 (22.3%)
Once every couple years	107 (18.8%)
Every day for a week	115 (20.2%)
Every day for a month	130 (22.8%)
Every day for a year	112 (19.7%)
Every day for a couple years	103 (18.1%)
Every day for the rest of your life	187 (32.9%)



## What side effects are you willing to risk for treatment of your cutaneous neurofibromas even if they may grow back later?



## How do you agree with the following statements?



# Effect of age, gender, family history

- Females were more likely to be bothered by cNF number ( $p=0.0006$ ; OR= 1.96 (1.34,2.92)) and appearance ( $p=0.0008$ ; OR= 1.99 (1.32,2.98)) than males but the percentage of individuals that have undergone current treatments and willingness to participate in experimental therapies were similar between sexes
- Older individuals (>50y) were more likely to have undergone surgical removal of cNFs ( $p=0.0001$ ; OR= 2.87 (1.82,4.51)) than younger individuals (18-49y) but the percentage of individuals that were very much or extremely bothered by cNFs and willingness to participate in experimental therapies were similar between age groups
- Responses were similar between individuals with a family history of NF1 and individuals that were the first person in the family diagnosed with NF1





# Higher burden of cNFs correlates most with treatment responses

cNF Views and Treatment	Respondents with 1-99 cNFs (%)	Respondents with 100+ cNFs (%)	Statistical Analysis
Acceptable minimum decrease in cNF number >50%	65.4	74.5	p=0.0468 OR=1.54 (1.00, 2.37)
Acceptable minimum decrease in cNF size >50%	63.5	72.6	p=0.0475 OR=1.53 (1.00, 2.32)
Have tried surgical removal of cNFs	47.3	76.5	p<0.0001 OR=3.63 (2.38, 5.52)
Willing to try surgical removal of cNFs	75.9	82.5	p=0.1017 OR=1.49 (0.92, 2.42)
Have tried laser removal of cNFs	3.7	12.8	p=0.0017 OR=3.84 (1.57, 9.41)
Willing to try surgical removal of cNFs	71.3	80.6	p=0.0293 OR=1.66 (1.05, 2.64)
Have tried radiofrequency ablation of cNFs	3.1	2.8	p=0.8689 OR=0.91 (0.28, 2.91)
Willing to try radiofrequency ablation of cNFs	58.8	70.9	p=0.0106 OR=1.71 (1.13, 2.58)
Have tried electrodesiccation of cNFs	5.5	14.5	p=0.0043 OR=2.91 (1.36, 6.21)
Willing to try electrodesiccation of cNFs	62.6	72.7	p=0.0293 OR=1.59 (1.04, 2.43)



# What might prevent you from participating in a clinical trial to treat your cutaneous neurofibromas?

- Themes:
  - Travel
  - Cost
  - Time off work/school
  - Eligibility (drug interactions/comorbidities)
  - Side-effects



# How do cNFs affect you?

- Themes:
  - Ridicule/staring- “Sometimes it's difficult to deal with the stares. It's not just one fibroma but many that invite the stares.”
  - Progressive nature- “The number continues to grow and grow... no end.”
  - Social isolation- “They all bother me. Every thing about this stupid NF1 bothers me. I work third shift so I don't have to see a lot of people.”
  - Intimacy issues- “It's been difficult to have and explore intimate relationships with men because of my body's appearance. I have been rejected because of the way my body looks.”
  - Self-image- “I look and feel like a monster;” “I feel like a genetic freak.”
  - ...



# Conclusions

- Appearance, number, location and size are the most bothersome cNF features
- Trunk and face are the most bothersome body areas
- Majority of respondents are okay with treatment that does not result in 100% clearance
- Most patients are willing to try current cNF treatments but are not aware of what is available
- The preferred modalities for experimental treatment are topical creams and oral medications
- No clear consensus for treatment frequency
- Higher burden of cNFs correlates most with treatment responses
- Limitations: not necessarily representative of the general population of individuals with NF1
- There were over 350 free text responses as to how and why cNFs affect the individual. A vast majority of responses touched on the psychosocial impact.



# Acknowledgements

- REiNS cNF Working Group
- REiNS Patient Representatives!
- UAB Biostatistics
  - Peng Li, PhD
- Funding
  - Francis S. Collins Award



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# QUESTIONS?

