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MYOTONIC
DYSTROPHY
FOUNDATION

Care and a Cure

Benefit and Risk in Myotonic Dystrophy: Patient Preference

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Patient Preference and Benefit-Risk

One of the most important questions asked by regulators is whether the clinical benefit of a drug outweighs its risk.



“...patient tolerance for risk and perspective on benefit, in addition to several other factors, may be considered in FDA’s assessment of the benefit-risk profile of certain devices when the information meets FDA’s standards for valid scientific evidence.”
-- Draft guidance on patient preference data in relation to devices issued by CDRH in May of 2015

Experiment Design Setup

“Max-Diff Analysis” or “Best/Worst Scaling”

- Each benefit was set up as a separate treatment against which a list of potential side effects was tested
- 8 separate treatments tested against 6 side effects
- Each treatment was reiterated several times per the Max-Diff formula:
 - $3K/k$ where K =total number of risks and k =number of risks displayed at a time
- Order in which items were presented to each survey respondent was randomized

TREATMENT 1 - IMPROVES MUSCLE STRENGTH

“Muscle Strength” describes the ability of your muscles to move against resistance in performing day to day activities. muscle strength affects your ability to walk, rise from a seated position, go up or down stairs and lift or hold objects.

Every treatment or therapy will have potential side effects or risks. Click the **best** and **worst** side effect or risk. By “**Best**” side effect or risk we mean the side effect or risk *you* are **most willing** to live with. By “**Worst**” side effect or risk we mean the side effect or risk you are **least willing** to live with. (Please choose one “**Best Risk**” *and* one “**Worst Risk**” in order to proceed) *

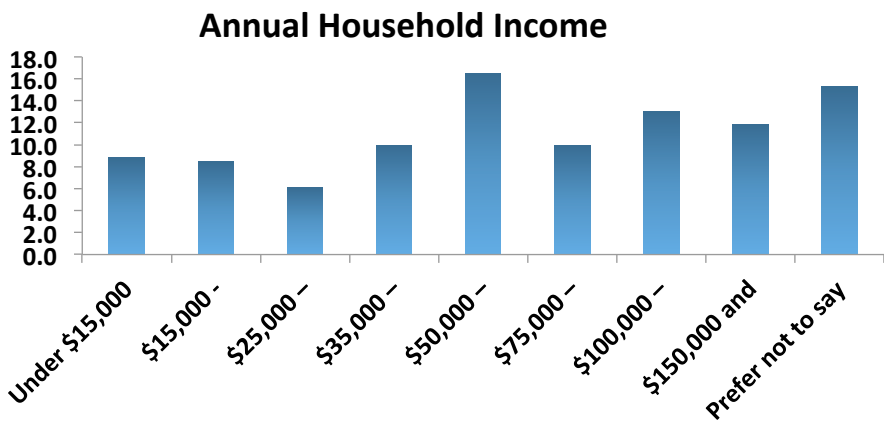
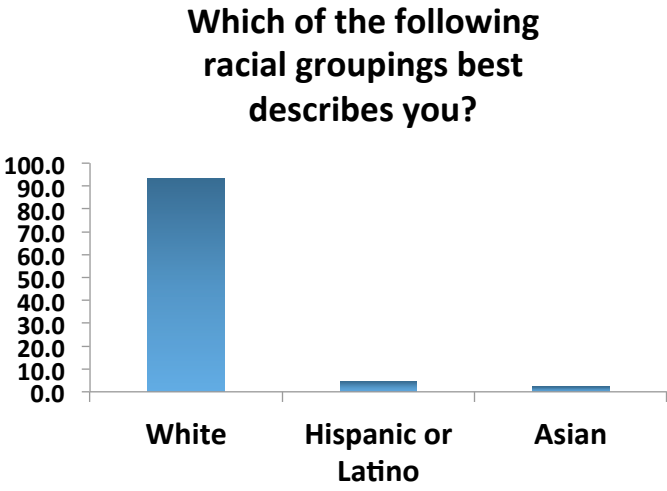
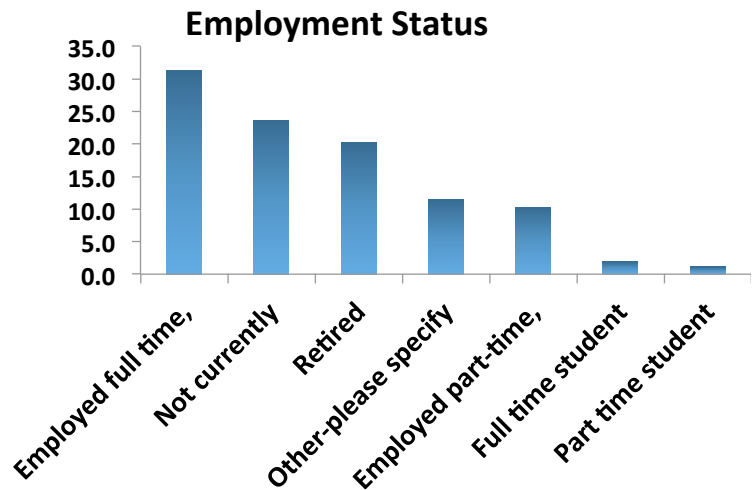
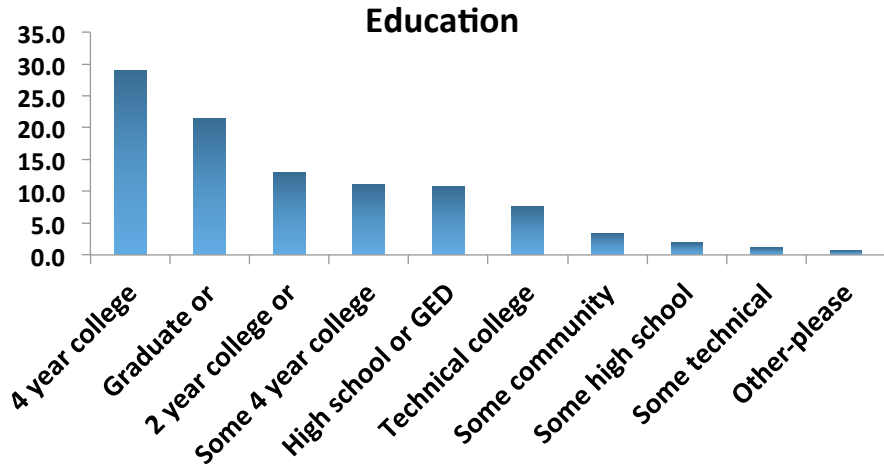
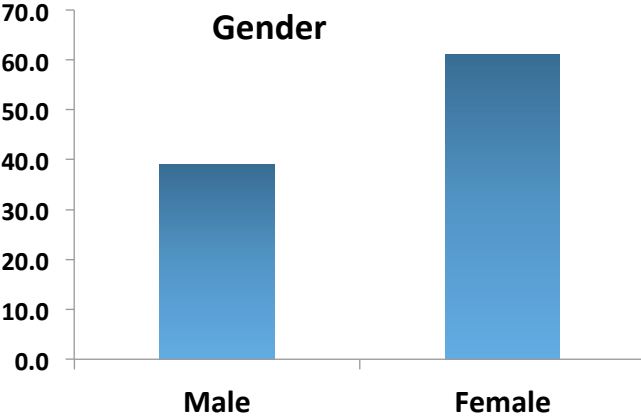
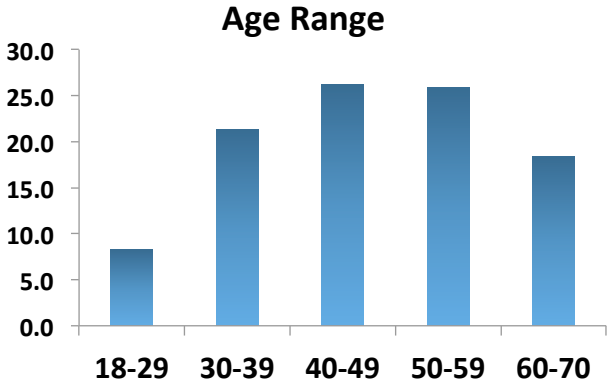
Best Risk	Side Effect of Treatment	Worst Risk
<input type="radio"/>	1 in 1,000 risk of liver failure	<input checked="" type="radio"/>
<input type="radio"/>	Loss of appetite is experienced by most people	<input type="radio"/>
<input checked="" type="radio"/>	Causes a small increase in tiredness during the day in most people	<input type="radio"/>
<input type="radio"/>	Loss of appetite with occasional vomiting is experienced by most people	<input type="radio"/>
<input type="radio"/>	Causes a large increase in tiredness during the day in most people	<input type="radio"/>

1 of 4 sets

Treatment/Risks Table

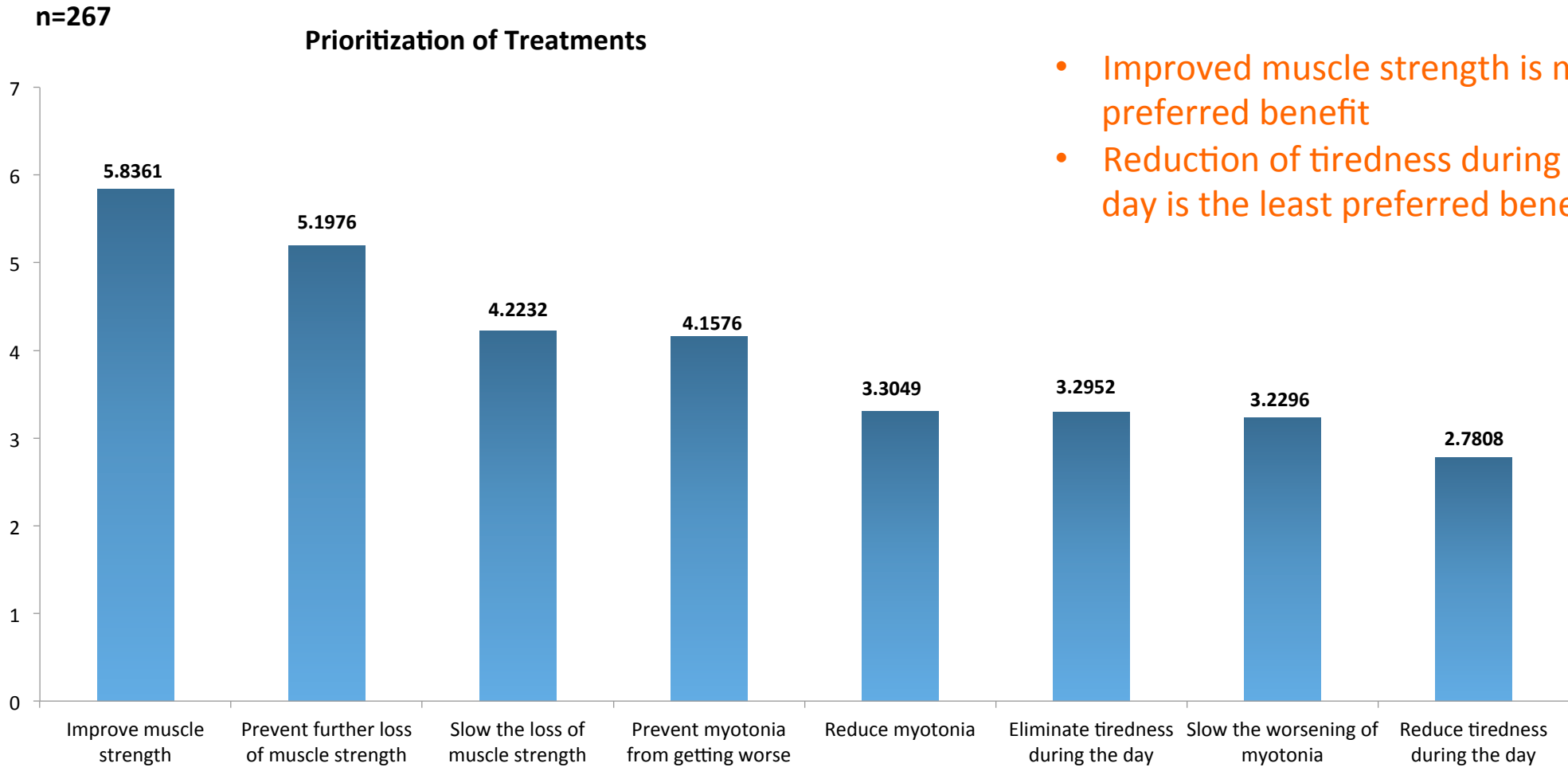
Treatments (Benefits)	Risks
Improves Muscle Strength	Loss of appetite is experienced by most people
Prevents Further Loss of Muscle Strength	Causes a small increase in tiredness during the day in most people
Slows the Loss of Muscle Strength	1 in 100,000 risk of liver failure
Eliminates Tiredness During the Day	Loss of appetite with occasional vomiting is experienced by most people
Reduces Tiredness During the Day	Causes a large increase in tiredness during the day in most people
Reduces Myotonia	1 in 1,000 risk of liver failure
Prevents Myotonia from Getting Worse	
Slows the Worsening of Myotonia	

Demographic Snapshot of Survey Respondents



n = 267

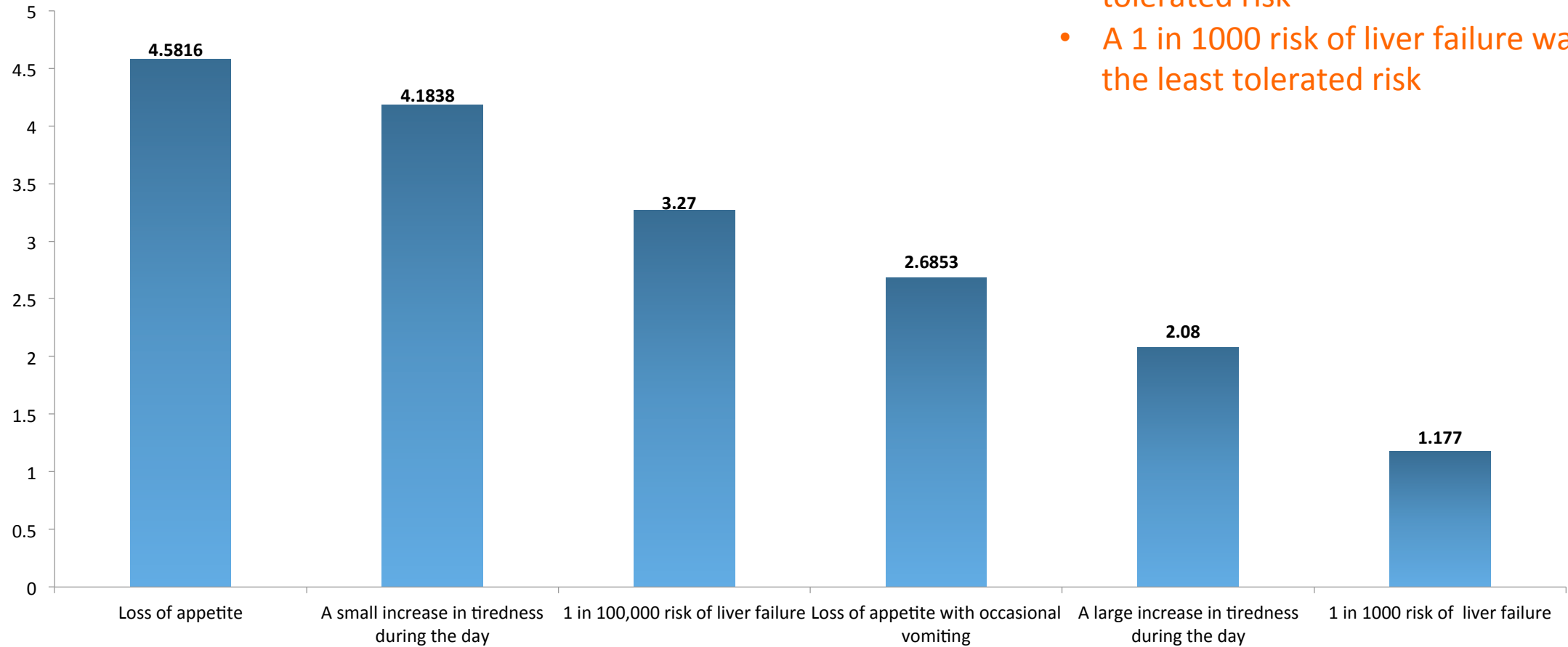
Overall Rank Ordering of Treatments or Benefits



- Improved muscle strength is most preferred benefit
- Reduction of tiredness during the day is the least preferred benefit

Overall Rank Ordering of Side Effects/Risks

Side Effects Most/Least willing to live with



- Loss of appetite was the most tolerated risk
- A 1 in 1000 risk of liver failure was the least tolerated risk

n=267

Impact of severity of symptoms on risk tolerance

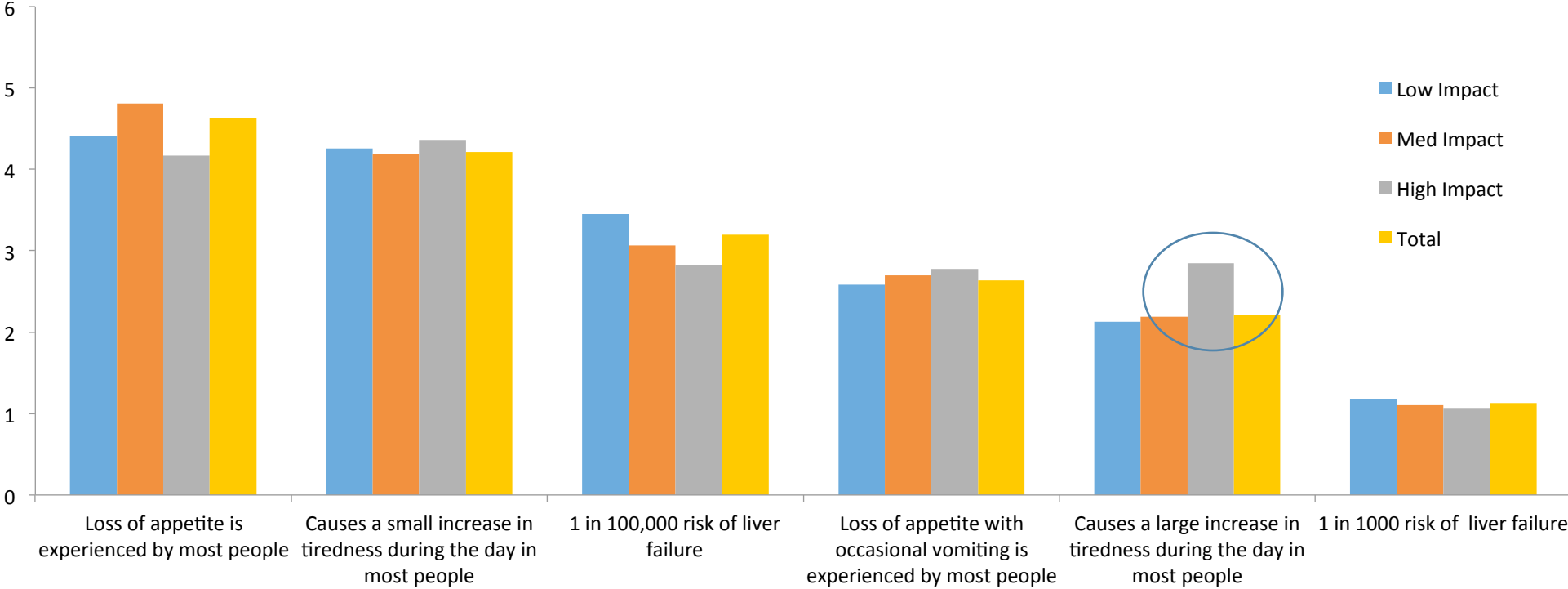
(Based on University of Rochester's MDH1 short form severity scale)



- People with DM1 in our study who had a high severity of symptoms (self-rated) were less tolerant of 1 in 1000 liver failure risk
- Those impacted with high severity of symptoms were also more willing to tolerate a large increase in tiredness through the day

Impact of Severity of Symptoms: Treatment 7

TREATMENT 7 - PREVENTS MYOTONIA FROM GETTING WORSE



n=267

People in the study who had a high severity of symptoms were more willing to accept a large increase in tiredness for any treatment that addresses myotonia

Conclusions

- Improving, halting or slowing muscle weakness were perceived to be of greatest benefit to the study participants
- Reducing fatigue was considered to be of least benefit
- Loss of appetite was the best tolerated risk and a 1:1000 chance of liver damage was the least tolerated
- The most severely impacted participants had a slightly higher tolerance for fatigue and a lower tolerance for potential liver damage
- The most severely impacted participants were more willing to tolerate fatigue as a side effect for a benefit related to slowing or reducing myotonia.
- There were very moderate effects due to numeracy and risk-taking aptitude.