

Parent Preferences for Delaying Progression of Type-1 Diabetes in Children: a Discrete Choice Experiment

PSI Webinar: Patient Preferences

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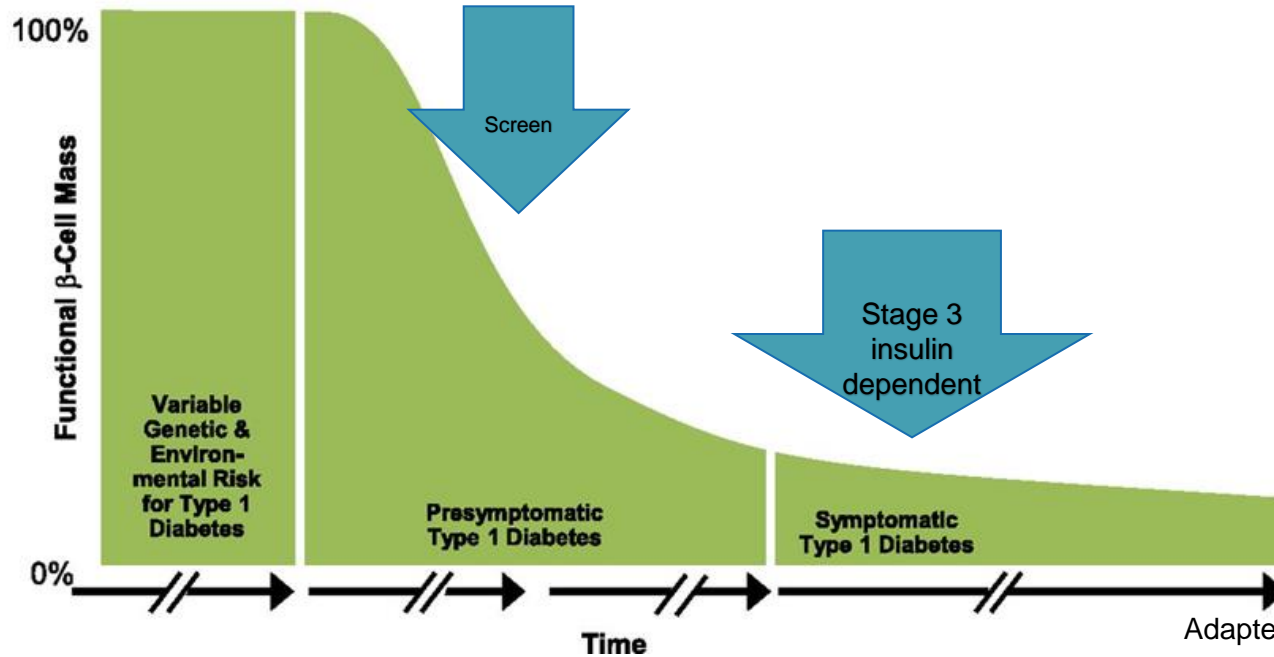
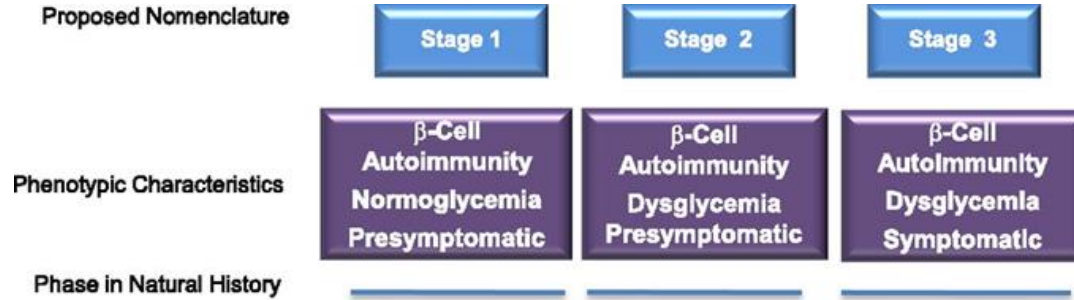
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- **R. DiSantostefano**
 - ▶ Employee of Janssen R&D, LLC
 - ▶ Shareholder of Johnson & Johnson
- **The survey was funded by Janssen, conducted in collaboration with RTI-Health Solutions**
- **Statements made in this presentation are those of the author and not necessarily those of her employer**

T1D Treatment Decision Context

- **If your child has a screening test and is at high risk of type-1 diabetes within a few years, do you:**
 - ▶ Consider a treatment to delay progression
 - ▶ Wait until you need exogenous insulin (Stage 3 – insulin dependent)
- **Choice has trade-offs of benefits and harms**
- **This is a preference-sensitive decision**

T1D: Disease Staging by Symptoms and Metabolic Criteria



Preference Study: Objectives

- **To quantify parent preferences, including benefit-risk tradeoffs, of a hypothetical therapy that delays onset of T1D in their children**
- **To investigate heterogeneity of these expressed preferences**
- **To utilize results to inform potential development and commercial strategy**

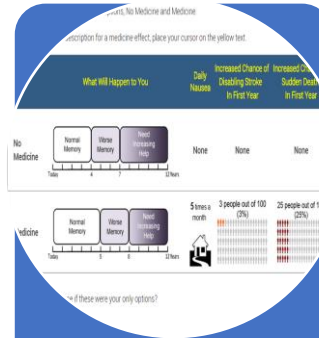
T1D Preference Research Approach



Step 1:
Engage T1D
patients,
parents and
JDRF



Step 2:
Perform qualitative
interviews



Step 3:
Conduct quantitative
preference
surveys



Step 4:
Assess benefit-risk
tradeoffs in
T1D



Study and Survey Designs

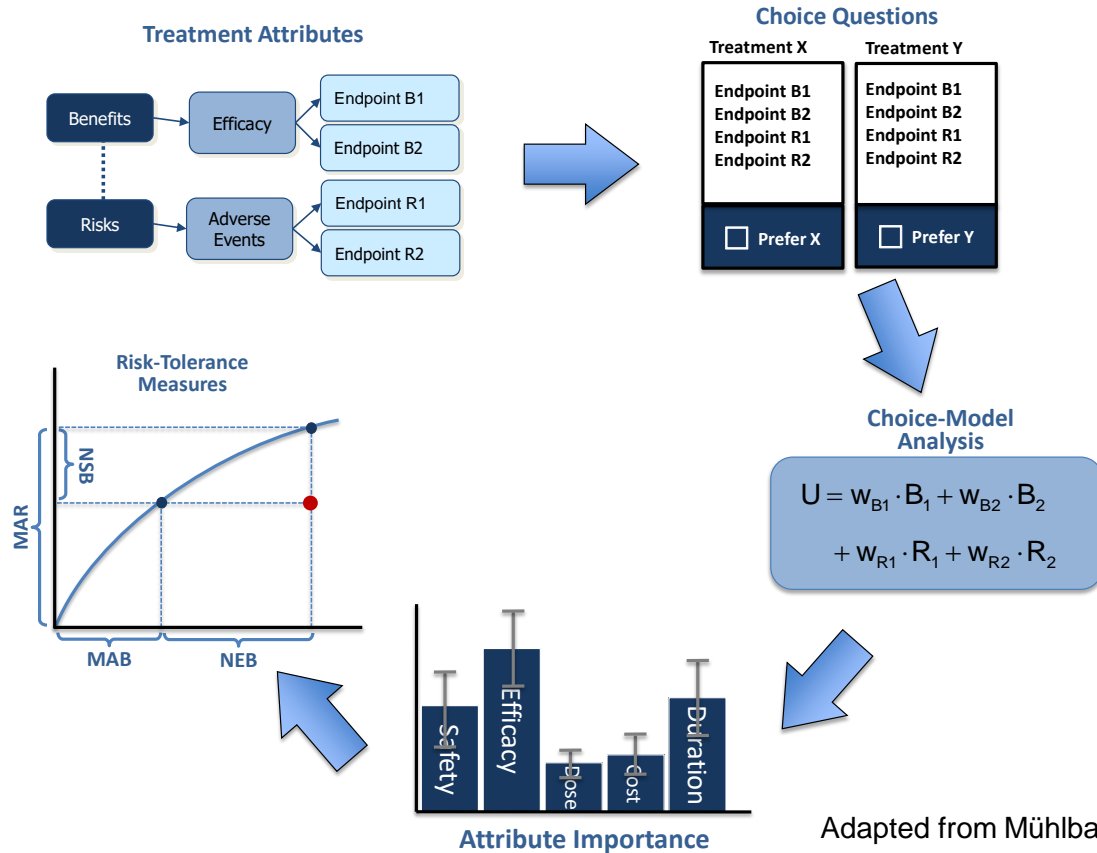
- **Qualitative Interviews (n=10) and pre-testing (n=15) to develop instrument**
- **US adults ≥ 18 years of age with children (n=1501)**
- **Stratified by**
 - ▶ Presence or absence of a child w/ T1D in family (n=601, n=900)
 - ▶ Age of youngest child (age 2-6, 7-10, 11-17 years)
- **Discrete-choice experiment**
- **8 trade-off questions**
 - ▶ 9 blocks chosen using a D-efficient design
 - ▶ Adult participants are told to assume their child will develop T1D (Stage III, insulin dependence) based on hypothetical biomarker screening within 6 mo. or 2 yrs
 - ▶ Choice between two treatments to delay progression or monitoring only
- **9th Dominant treatment question**

Attributes and Levels in Experiment

Attribute	Levels
Time until insulin dependence	6 years [if group 2] or 4 ½ years [if group 1] until insulin dependence
	4 ½ years [if group 2] or 3 years [if group 1] until insulin dependence
	2 ½ years [if group 2] or 1 year [if group 1] until insulin dependence
Reduces chance of long-term health complications by 50%?	Yes
	No
Chance of hospitalization due to DKA when become insulin dependent	None
	1% 1 out of 100 children
	4% 4 out of 100 children
	5% 5 out of 100 children
Chance of serious infection from the treatment	None
	2% 2 out of 100 children
	6% 6 out of 100 children
Skin reaction from the treatment for several days each month	No
	Yes
3 days of nausea a month for first 3 months	None
	Mild
	Moderate

Note: Baseline randomization: group 2 = 2 years until insulin dependence, group 1 = 6 months until insulin dependence.

Steps for Benefit-Risk Preference Study



Adapted from Mühlbacher, 2011

Which treatment option would you choose for your child?

Treatment Feature	Treatment A and Monitoring	Treatment B and Monitoring	Monitoring Only
Time until insulin dependence	6 years until insulin dependence	4 ½ years until insulin dependence	2 years until insulin dependence
Reduces chance of long-term health complications by 50%?	No	Yes	No
Chance of hospitalization due to DKA when become insulin dependent	None	1% 1 out of 100 children	5% 5 out of 100 children
Chance of serious infection from the treatment	6% 6 out of 100 children	2% 2 out of 100 children	None
Skin reaction from the treatment for several days each month	Yes	Yes	No
3 days of nausea a month for first 3 months	Moderate	None	None
Which would you choose for your child?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Respondents chose between 2 hypothetical treatments or an opt-out (Monitoring only) in a series of choice questions.

Which treatment option would you choose for your child?

Treatment Feature	Treatment A and Monitoring	Treatment B and Monitoring	Monitoring Only
Time until insulin dependence	4½ years, until insulin dependence	1 year until insulin dependence	6 months until insulin dependence
Reduces chance of long-term health complications by 50%?	Yes	No	No
Chance of hospitalization due to DKA when become insulin dependent	None	5% 5 out of 100 children	5% 5 out of 100 children
Chance of serious infection from the treatment	None	6% 6 out of 100 children	None
Skin reaction from the treatment for several days each month	No	Yes	No
3 days of nausea a month for first 3 months	None	Moderate	None
Which would you choose?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Dominant Choice Question

- A DCE-type comprehension question where one treatment option was better than another in terms of benefits and harms (e.g., Treatment A)
- We insert choices like this to check attendance to the question, risk understanding, etc.

Choice Model Specifications

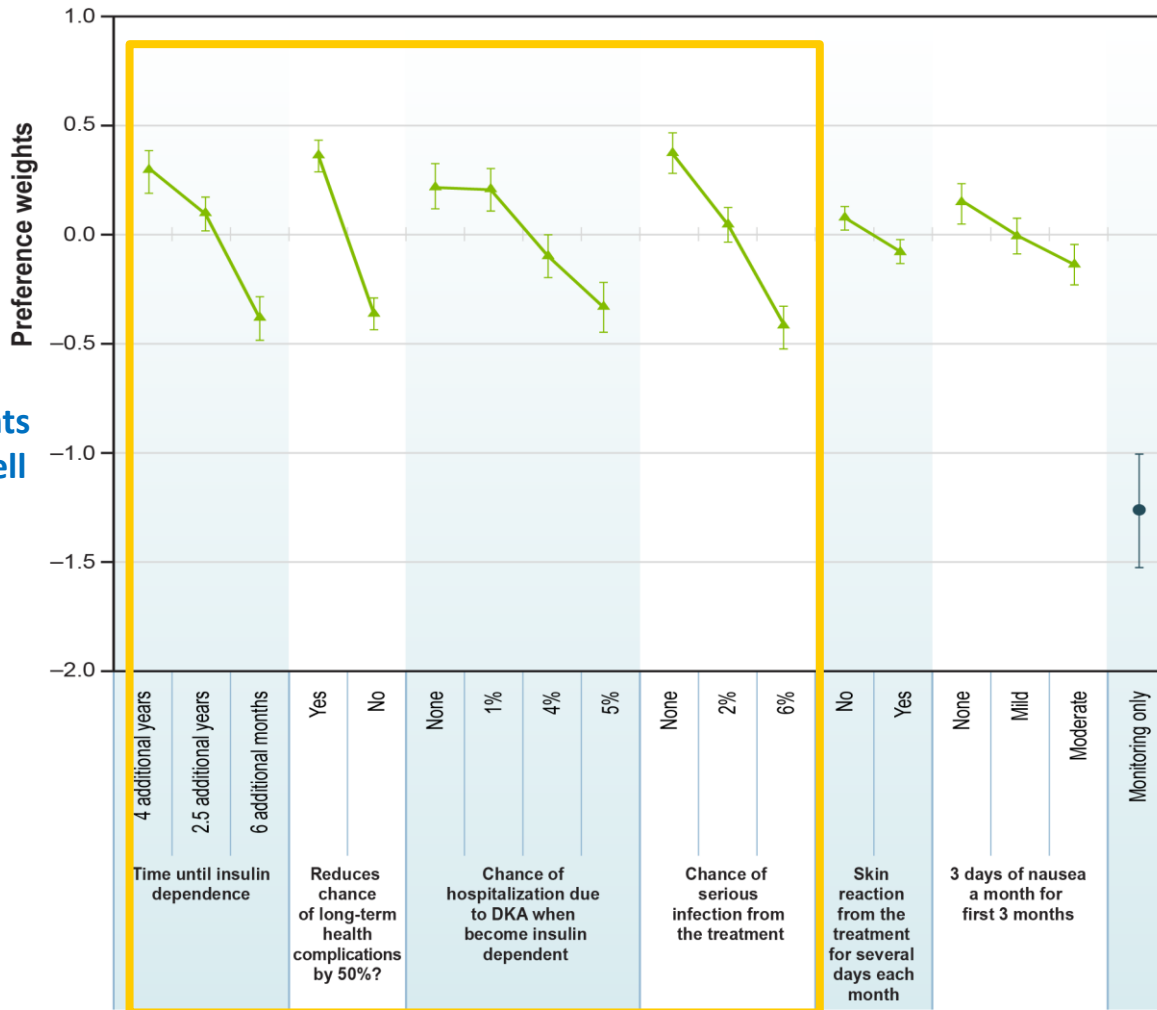
- **Taste heterogeneity**

- ▶ Random-parameters logit (RPL); taste heterogeneity modeled as normal distributions (child with T1D, without T1D separately)
- ▶ Latent-class analysis (LCA); taste heterogeneity modeled as discrete classes with similar preferences (child with T1D, without T1D combined)

- **RPL**

- ▶ Effects cell coding for each attribute
- ▶ Alternative specific constant for Monitoring Only that captured “no delay”
- ▶ Log-odds parameter estimates to facilitate comparisons

Parents of children with T1D Preference Weights (N=600)



Better outcomes have significantly higher weights

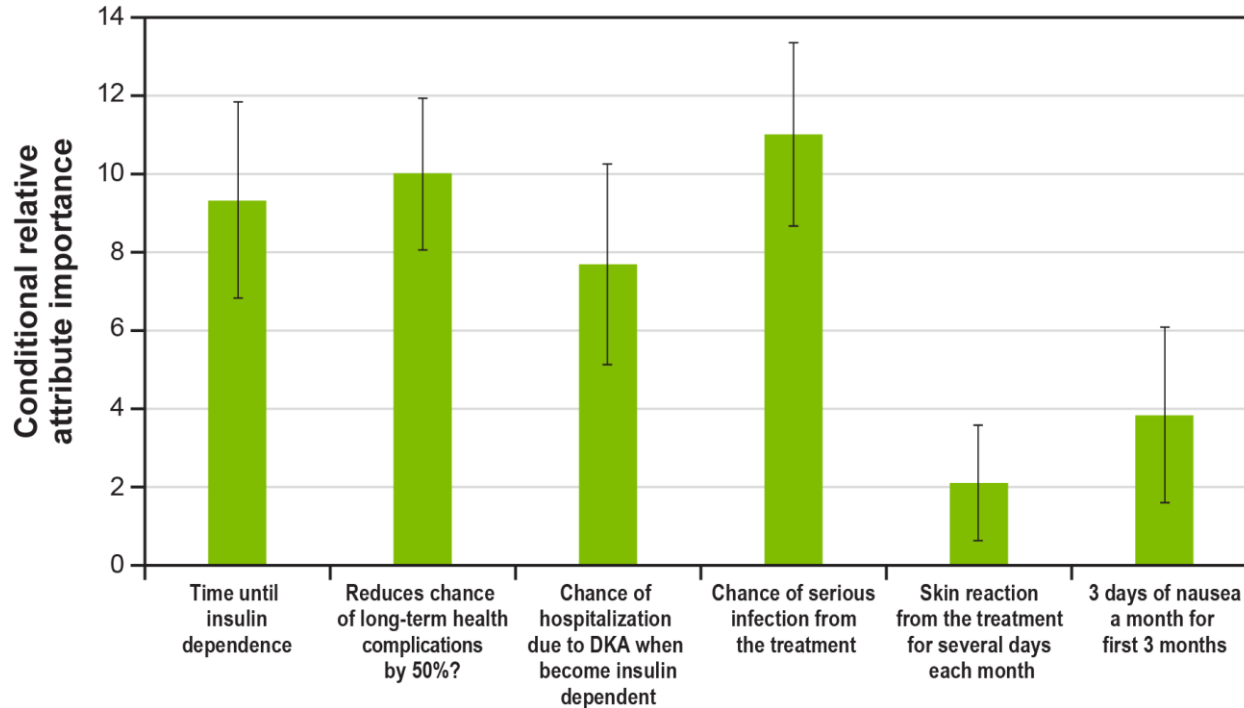
Worse outcomes have significantly lower weights

Most important attributes have largest difference between highest and lowest coefficients

RPL: Coefficients from Effects Cell Coding

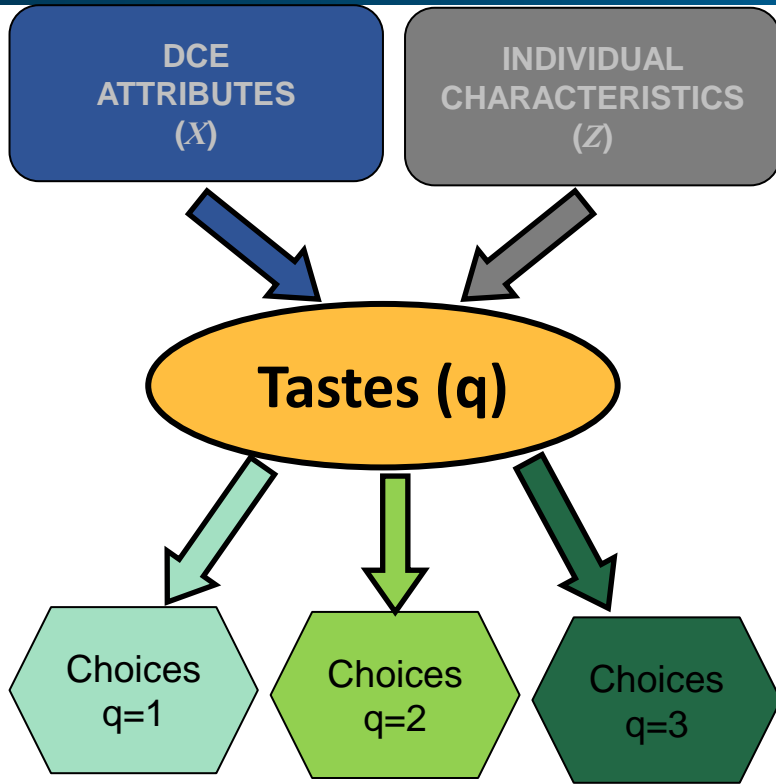
Parents of children with T1D

Conditional Relative Importance of Attributes for a Change from Most Preferred to Least Preferred Level (N=600)



Note: Conditional relative importance scores are scaled so that conditional relative importance of reducing the chance of long-term health complications by 50% (LTR) is equal to 10, and all other scores are relative to LTR.

Latent-Class Analysis



Latent-class analysis (LCA)

- Subset of structural equation modeling
- Finds unobserved or latent groups of cases in multivariate categorical data
- Membership probabilities are tabulated and group characteristics are examined

Software: Latent GOLD®

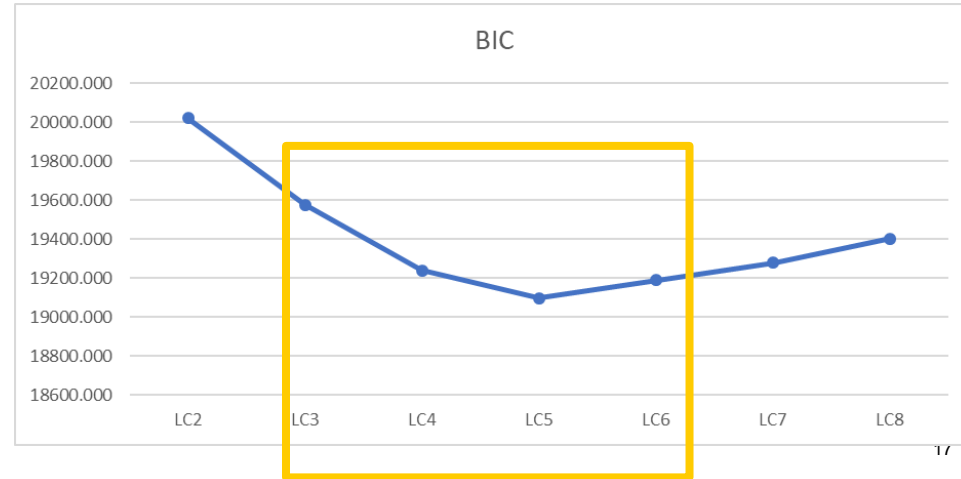
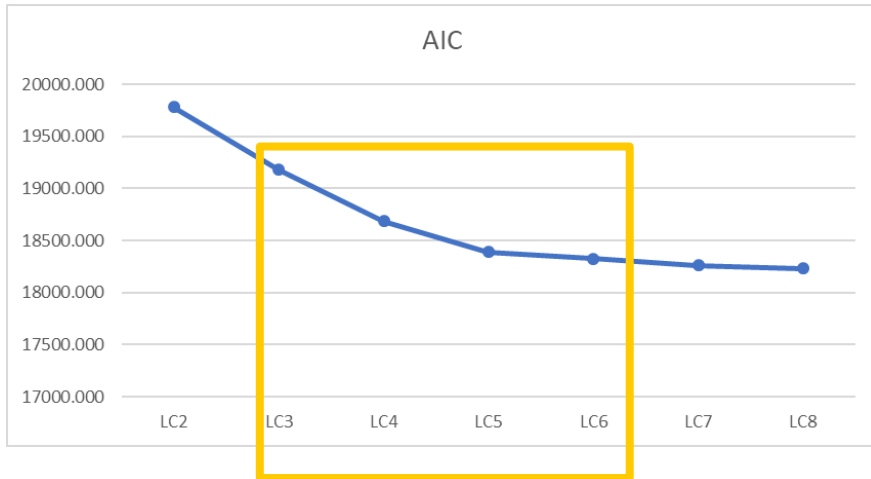
(Statistical Innovations, Arlington, MA)

Model Variables

- **Discrete choices responses (X)**
- **Additional respondent-specific covariates (Z)**
 - ▶ Has a child with T1D
 - ▶ Is female
 - ▶ Age 40 or older
 - ▶ No insurance or has Medicaid
 - ▶ 4-year college degree or more
 - ▶ Child is age 2 years to 6 years, inclusive
 - ▶ Failed the risk comprehension question and the dominated choice question
 - ▶ Subjective numeracy score (SNS, Fagerlin et al, 2007)

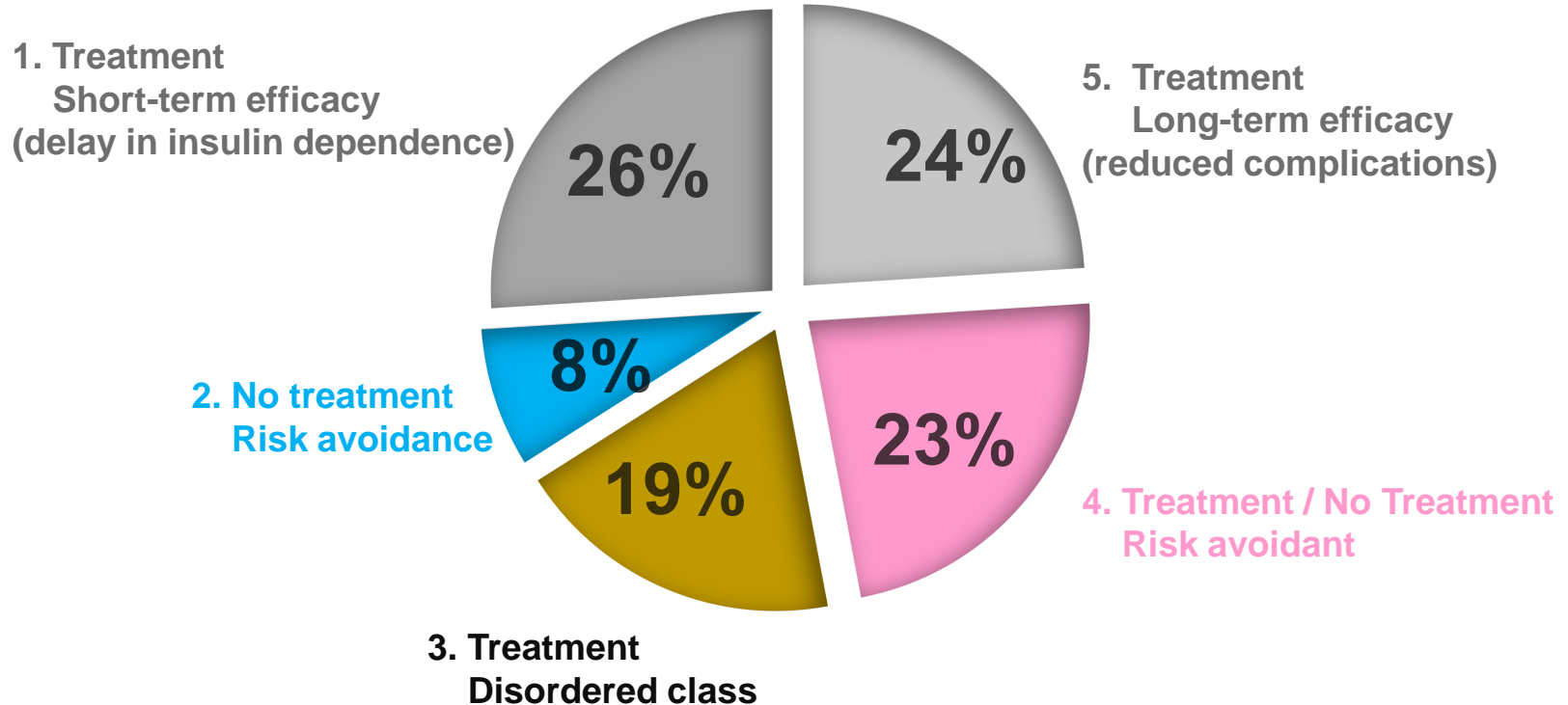
Latent Class Modeling Considerations

- **Selected final latent class models for evaluation using**
 - ▶ AIC/BIC criteria (2-8 classes classes)
 - ▶ Evaluation of 3-, 4-, and 5- class models
 - ▶ Kept 5-class model



Latent Class Analysis Revealed 5 Classes With Unique Preferences

Membership probability % for each class is shown



Results Summary (N=1499)

5-Class Model

Class	Mean probability of class membership	Key Preferences	Compared to Class 5, respondents Significant differences shown, $p \leq 0.05$
1	26% Treatment, Short-term efficacy	<ul style="list-style-type: none"> Prefer treatment over monitoring Time until insulin dependence (largest relative importance) 	<ul style="list-style-type: none"> Not different from class 5
2	8% Risk focus, monitor	<ul style="list-style-type: none"> Prefers monitoring only Dislikes all risks 	<p>Are more likely to:</p> <ul style="list-style-type: none"> have a child w/ T1D have lower self-reported numeracy <p>Are less likely to:</p> <ul style="list-style-type: none"> have 4-year college degree or more
3	19% No treatment, Risk avoidance	<ul style="list-style-type: none"> Prefer treatment over monitoring Disordered preferences for time until insulin dependence, skin reaction, and nausea 	<p>Are more likely to</p> <ul style="list-style-type: none"> have a child w/ T1D be male have Medicaid or no insurance have failed both risk grid comprehension & dominated choice questions
4	23% Trt / No Trtment Risk avoidant	<ul style="list-style-type: none"> Avoiding the risk of serious infection (largest relative importance) Preference for monitoring only higher than classes 1,3, & 5 Dislikes all risks 	<p>More likely to</p> <ul style="list-style-type: none"> have a child with T1D have lower self-reported numeracy
5	24% Treatment, Long-term efficacy	<ul style="list-style-type: none"> Prefer treatment over monitoring Reducing the chance of long-term health complications by 50% (largest relative importance) 	<ul style="list-style-type: none"> Baseline class

Limitations

- **Convenience sample**
- **Some recoding bias: choosing a treatment vs. monitoring ('do something' vs. 'do nothing')**
- **External factors that affect treatment decisions were not considered (e.g., price, physician discussion)**
- **Despite limitations, results inform**
 - ▶ Development strategy
 - ▶ B-R tradeoffs and heterogeneity
 - ▶ Regulators

References

ISPOR Conjoint Analysis Good Research Practices Task Force Available on ISPOR Website, published in Value in Health

- Hauber, 2016. Statistical methods for the analysis of discrete choice experiments
- Johnson, 2013. Constructing experimental designs for discrete-choice experiments
- Bridges, 2011. Conjoint analysis applications in health—a checklist

Publication of T1D preference study

- DiSantostefano RL. Diabetes Technol Ther. 2020 Aug;22(8):584-593.

Acknowledgements & Discussion

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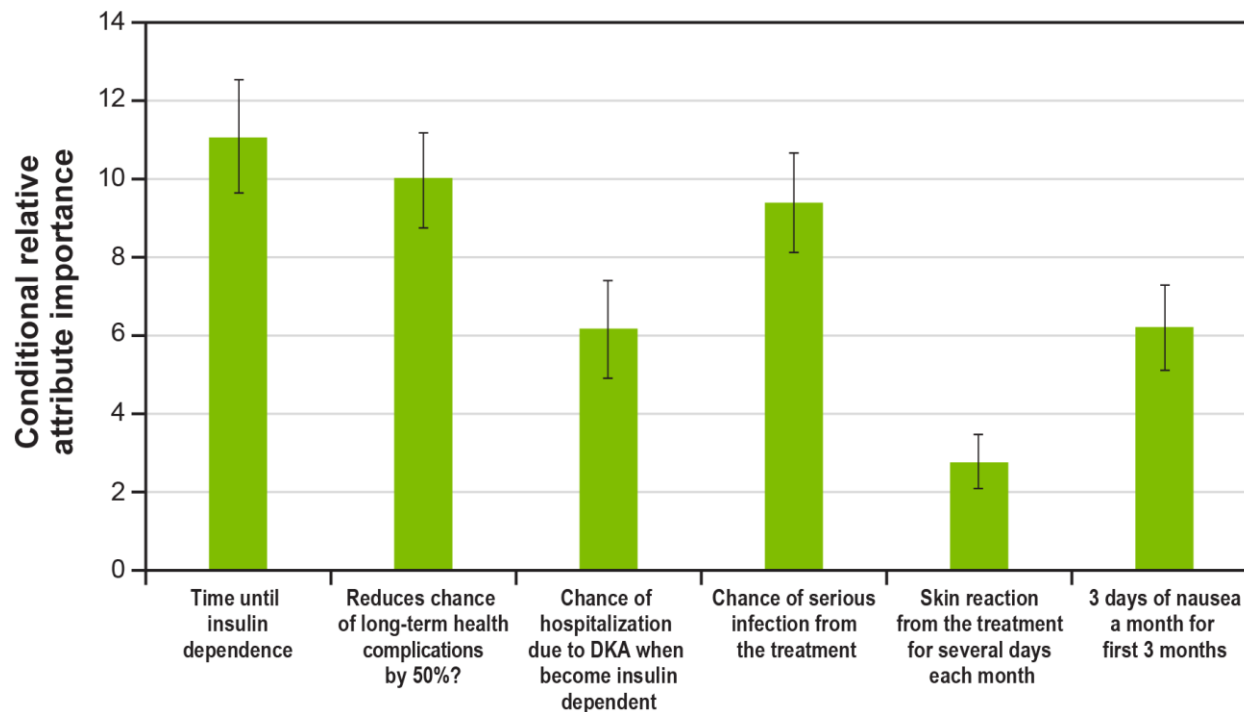
- Joseph Hedrick

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Parents of children without T1D

Conditional Relative Importance of Attributes for a Change from Most Preferred to Least Preferred Level (N=901)



Note: Conditional relative importance scores are scaled so that conditional relative importance of reducing the chance of long-term health complications by 50% (LTR) is equal to 10, and all other scores are relative to LTR.

Tradeoffs: Maximum Acceptable Risk (MAR)

- MAR of serious infection for improvements in time until insulin dependence.

Table 1. Maximum Acceptable Risk of Serious Infection: Additional Time Until Insulin Dependence

Without T1D			MAR of Serious Infection
Benefit	From	To	(95% CI)
Time until insulin dependence	6 additional months	2.5 additional years	5.2% (4.4%–6.0%)
	2.5 additional years	4 additional years	2.0% (1.1%–2.9%)
	6 additional months	4 additional years	7.2% (5.9%–8.6%)
With T1D			MAR of Serious Infection
Benefit	From	To	(95% CI)
Time until insulin dependence	6 additional months	2.5 additional years	3.3% (1.7%–4.9%)
	2.5 additional years	4 additional years	1.2% (0.2%–2.2%)
	6 additional months	4 additional years	4.5% (2.5%–6.5%)

- Parents without a child with T1D will accept a higher chance of serious infection than parents of a child with T1D in exchange for improvements in efficacy.