WHY THE FDA INTEREST IN PATIENT PREFERENCE?: WEIGHING RISKS AND BENEFITS OF INNOVATIVE LIMB PROSTHETICS

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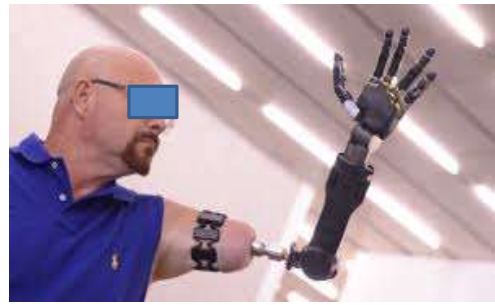
PATIENT PREFERENCES: BREAKING NEW GROUND IN REGULATORY SCIENCES

- **Patient groups demanding voice in regulatory and medical decisions**
- **FDA stated they will consider patient preference in drug and device benefit/risk decisions**
  - FDA published a Patient Preference Information Guidance
  - CBER & CDER include patient preference information as a goal to patient-focused drug development
  - Urgent need for more examples to inform decisions: Obesity, Duchenne's, MS, Retinal Disease, Renal Replacement devices, Islet cell transplant
  - Must meet scientific rigor : DISCRETE CHOICE MODELS
- **UCSF/Stanford CERSI center: Major role in Education and Science of Discrete Choice**
- **Our studies provide MODELS of technique and validity for regulatory decisions**
  - **Osseointegration and myolectric control in prosthetics**
  - **Renal Replacement Therapies**
  - **Islet cell transplant in T1Diabetes**

A MODEL OF VALID PATIENT PREFERENCE MEASUREMENT: LUKE SKYWALKER PROSTHETICS



- Rapid innovation in new prosthetic devices is astonishing
- By 2020, 2.2 million people with limb loss
- 70% don't use their prosthetic device

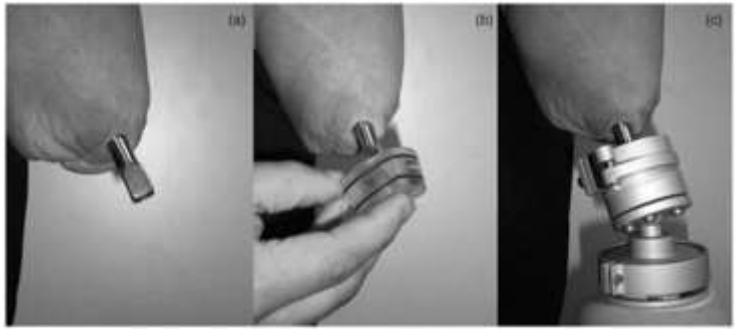
PROSTHETIC ADOPTION IS HIGHLY PREFERENCE SENSITIVE

IT IS ESSENTIAL TO KNOW HOW PATIENTS WEIGH RISKS AND BENEFITS

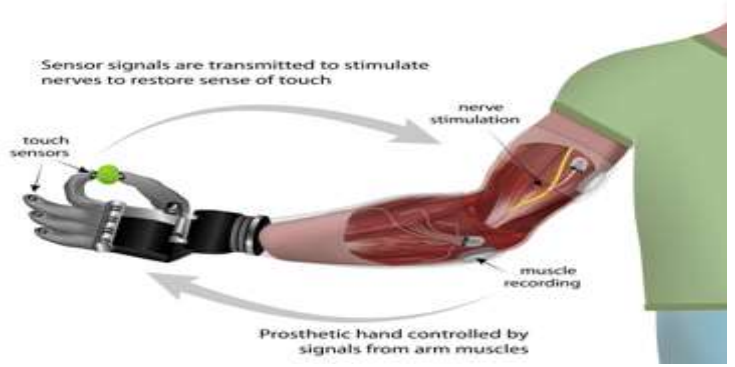
OF NEW PROSTHETIC DEVICES FOR REGULATORY DECISIONS

<u>OBJECTIVE:</u> Determine how patients weigh risks/benefits of 2 prosthetic innovations & test validity for regulatory decisions

Osseointegration



Myoelectric Control



PATIENT PREFERENCE MEASUREMENT: DISCRETE CHOICE

Attributes	Device A	Device B
Percent who experience daily pain	2 in 10	0 in 10
Independence in cooking dinner	Completely independent	Not independent at all
Number of grip patterns, providing different strengths and smoothness of motion	8 grip patterns, full strength and fluid motion	2 grip patterns, little strength and choppy motions
Chance of having a serious but treatable infection	1/100	No chance
WHICH DEVICE WOULD YOU CHOOSE ?		

Attributes	Device A	Device B
Percent who experience daily pain	2 in 10	0 in 10
Independence in cooking dinner	Completely independent	Not independent at all
Number of grip patterns, providing different strengths and smoothness of motion	8 grip patterns, full strength and fluid motion	2 grip patterns, little strength and choppy motions
Chance of having a serious but treatable infection	50/100	No chance
WHICH DEVICE WOULD YOU CHOOSE ?		

Progress: Patient Preferences for Risks/ Benefits of Osseointegration Prosthetics: Patients with Upper Limb Loss

Sample

- We surveyed 25 adults with at least one ULL above the wrist.
- Recruited from: Amputee Coalition, UCSF Prosthetic Clinics, VA Medical Centers, Social media (Instagram and Reddit)
- Surveys administered by computer either in-person or online with video chat

Innovations Tested

Osseointegration
Myoelectric Control

Design: Choice Based Conjoint Approach (CBC)

- Sawtooth Software: random, full profile, balanced overlap design
- 18 choice-paired questions, with opt out question post forced choice

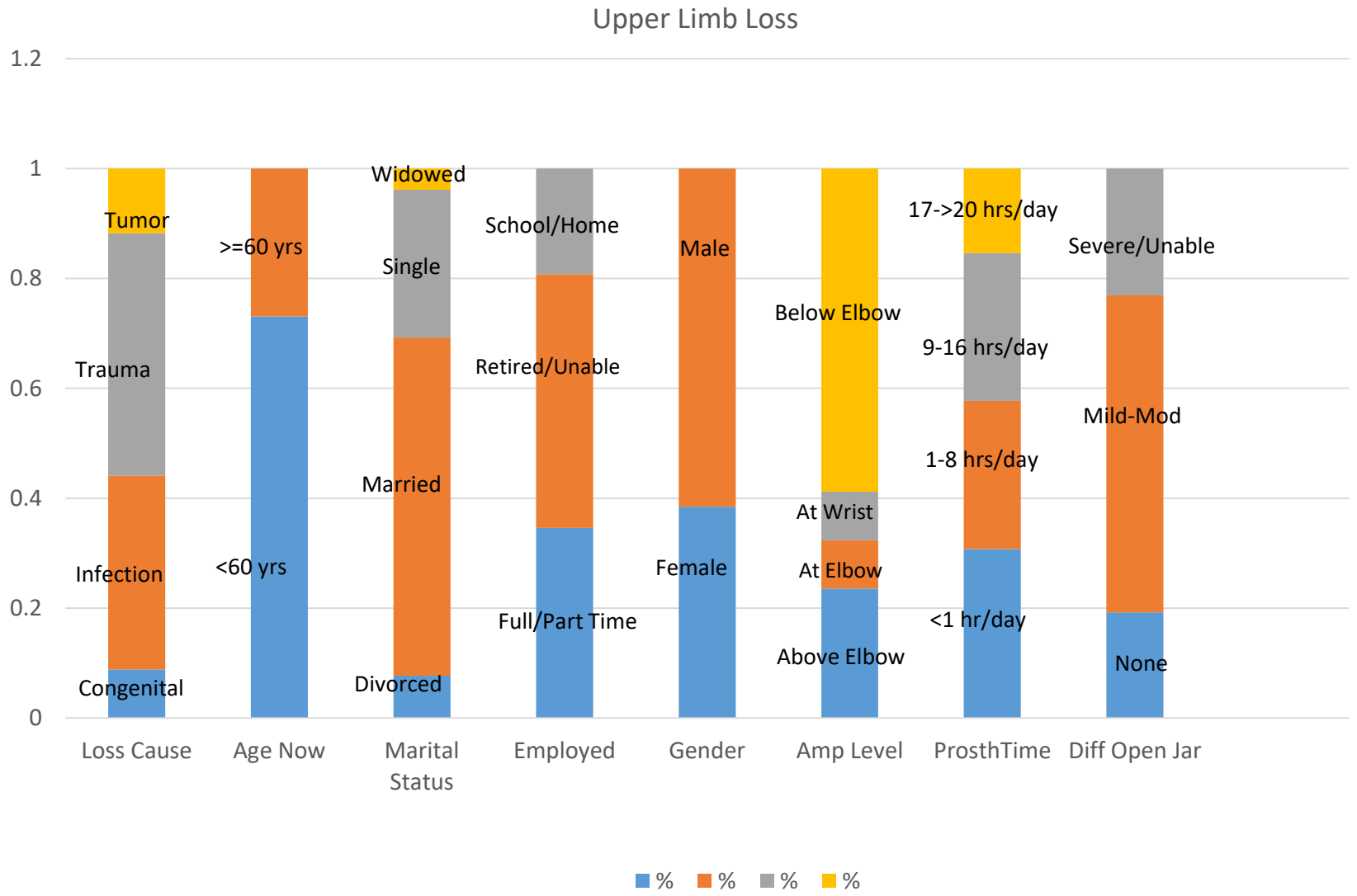
Analysis:

- Mixed effects logistic regression calculated beta coefficients as part-worth utilities to reflect preferences.

ULL Choice Based Conjoint Measure
Used Video to Show Complex Motions

FEATURES	Option 1	Option 2
Chance of daily pain/discomfort is:	2 in 10	6 in 10
Independence in cooking dinner:	Need some help 	Completely independent 
Ease of prosthetic use:	No heavy socket and harness	Easily clips onto screw in bone
Chance of serious but treatable infection is:	10 in 100 	0 in 100 
Prosthetic feels connected to your body:	Does not feel connected	Feels somewhat connected
Able to feel touch sensations:	No sensations	Feel object is rough or smooth
A failure results in no prosthetic for 5 years in:	0 in 100 	40 in 100 
Surgery or procedures needed:	Two hospital surgeries	One clinic procedure
Grip patterns, strength and motion:	Two grip patterns, little strength and choppy motion 	Four grip patterns, moderate strength and motion 
Choose one:	○	○

CHARACTERISTICS OF PERSONS WITH UPPER LIMB LOSS (N=23)



RESULTS: PREFERENCE SCORES FOR RISKS AND BENEFITS OF DEVICE (N=23)

- Compared with inability to **COOK DINNER INDEPENDENTLY**, needing some help increases preference by 1.11 & complete independence by 1.70
- After **2 GRIP PATTERNS**, preference for **4 GRIP PATTERNS** is greater (1.37) than for **8** (1.23)
- Preference for **NO SKIN PROBLEMS** is 0.60, and **EASY ATTACHMENT** is 0.59
- Each 10% increase in **CHANCE OF DAILY PAIN** decreases preference by 1.47
- Each 1% increase in **TREATABLE INFECTION** decreases preference by 0.15.
- Each 1% increase in **DEVICE FAILURE FOR 5 YRS** decreases preference by 0.65
- Compared to none, **2 HOSPITAL SURGERIES** decreases preference by 0.58 and **4 SURGERIES** by 1.08.
- **FEELING CONNECTED** & **SENSATION** are not important.

Attribute	*β - coefficient*	*SE*	*95% CI*	*P-value*
PAIN	-1.47	0.33	-2.12 to -0.82	<0.001
DINNER: Not independent at all	Reference	-	-	-
Need some help	1.11	0.20	0.71 to 1.50	<0.001
Completely independent	1.70	0.21	1.29 to 2.11	<0.001
EASE: Heavy socket and harness	Reference	-	-	-
Easily clips onto screw in bone	0.59	0.23	0.14 to 1.05	0.01
No skin problems	0.60	0.23	0.14 to 1.06	0.01
No heavy socket and harness	0.31	0.23	-0.15 to 0.76	0.18
INFECTIONS TREATABLE	-0.15	0.04	-0.23 to -0.08	<0.001
CONNECTED: Not feel connected	Reference	-	-	-
Feels somewhat connected	0.18	0.20	-0.22 to 0.57	0.37
Feels connected like normal arm	0.33	0.20	-0.07 to 0.72	0.10
TOUCH: No sensations	Reference	-	-	-
Barely feel object	-0.33	0.20	-0.73 to 0.06	0.10
Feel object is rough or smooth	0.02	0.20	-0.38 to 0.41	0.94
FAILED DEVICE 5 YEARS	-0.65	0.50	-1.63 to 0.34	0.20
PROCEDURES: None	Reference	-	-	-
One clinic procedure	-0.15	0.23	-0.60 to 0.30	0.52
Two hospital surgeries	-0.58	0.23	-1.03 to -.013	0.01
Four hospital surgeries	-1.09	0.23	-1.54 to -0.63	<0.001
GRIPS: Two pattern grip	Reference	-	-	-
Four pattern grip	1.37	0.21	0.97 to 1.77	<0.001
Eight pattern grip	1.23	0.20	0.83 to 1.63	<0.001

OPRA PRO study results VS CBC PPI results: Persons w/ LLL seem to care more about risks than benefits https://www.accessdata.fda.gov/cdrh_docs/pdf8/H080004B.pdf (n=65)

- **BENEFITS:**

❑ Improved range of movement around the hip joint, as motic was unimpeded by a socket brim. This was demonstrated by increased range of motion scores from baseline to 24 months;

❑ Increased prosthetic use, level of function and mobility, including longer walking distances and increased sitting comfort as demonstrated by improvements in Q-TFA subscores;

❑ Improved quality of life as demonstrated by the Q-TFA;

❑ Reduced socket related soft tissue problems;

- **RISKS:**

❑ Infection: 31 (61%) subjects with 44 events: o Superficial infection: 28 (55%) subjects with 40 events o Deep infection 3 (6%) subjects with 4 events

❑ Mechanical complication of the implant: 4 (8%) subjects wit 9 events

❑ Pain: 6 (12%) subjects with 6 events

❑ Injury: 4 (8%) subjects with 4 events.

Attribute	*Odds Ratio*	*β - coefficient*	*SE*	*95% CI*	*P-value*
Serious infection	0.1840	-1.69	0.22	-2.12 to -1.26	<0.001
Complete failure rate	0.2253	-1.49	0.27	-2.03 to -0.95	<0.001
Time without prosthetic					
No time without prosthetic		Reference	-	-	-
9 months	0.3718	-0.99	0.11	-1.20 to -0.77	<0.001
4 months	0.5258	-0.64	0.11	-0.86 to -0.43	<0.001
Activity Limitations					
No limitations		Reference	-	-	-
No impact sports	0.5230	-0.65	0.13	-0.89 to -0.40	<0.001
No public pools	0.5757	-0.55	0.13	-0.80 to -0.31	<0.001
No excess pivots or twists	0.6816	-0.38	0.12	-0.63 to -0.14	0.002
Avoid socket problems					
No sensations		Reference	-	-	-
Avoid socket perspiring, skin chafing, and weight	1.2577	0.21	0.12	-0.03 to 0.46	0.09
Rapid snap on	1.3305	0.29	0.13	0.04 to 0.53	0.02
Comfort sitting	1.3764	0.32	0.12	0.08 to 0.56	0.01
Sense of limb perception					
No sense of limb		Reference	-	-	-
Feel somewhat sense of limb	1.2322	0.21	0.11	-0.003 to 0.42	0.053
Feels connected like normal limb	1.5746	0.45	0.11	0.24 to 0.67	<0.001
Improved motion and fatigue					
Almost normal walking gait		Reference	-	-	-
Easily maneuver leg into car or under a table	0.9145	-0.09	0.12	-0.33 to 0.15	0.47
Need fewer or no aides on uneven ground	0.8199	-0.20	0.13	-0.44 to 0.05	0.11
Daily walks longer with less fatigue	0.0160	-0.09	0.13	-0.33 to 0.16	0.49
Chance of daily pain	0.2145	-1.54	0.18	-1.89 to -1.19	<0.001

FDA IMPACT: VALUE AND CHALLENGES

- PPI INFORMATION CAN:
  - Support FDA risk benefit decisions: Sub analysis can target risk to those that benefit most
  - Inform FDA Guidences: Define PPI study scientific quality
  - Support patient advocacy for rare diseases
  - Inform drug/device development & clinical trial outcomes
- CHALLENGES
  - Lack of consensus on the definition and scope of PPI (scientific patient input, not just a patient survey)
  - Lack of agreement on methods which meet needs of patients and FDA
  - Shortage of Experts and Funding
- CERSI CENTERS PLAY MAJOR ROLE: Goals to advance regulatory science through innovative research, education, and scientific exchanges
  - U. MD,. UCSF-Stanford, Johns Hopkins U., Yale-Mayo Clinic (centers of excellence in regulatory science)