Patient Perspectives on Osseointegration: A National Survey of Veterans with Upper Limb Amputation

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Abstract

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Introduction: Osseointegrated (OI) prostheses have a unique benefit-risk profile among prosthetic alternatives and have been marketed in the U.S. under a Humanitarian Device Exemption since 2015. Information about upper limb prosthesis user perspectives on benefits and risks, prosthesis-user subpopulations for whom OI is most acceptable, and outcomes that matter most to patients could help inform clinical and regulatory decision-making. Recent 21st Century Cures legislation expanded the role of patient experience data in the FDA decision-making process, recognizing that patient perspectives may be informative to regulators.

Objective: To better understand prosthesis user perspectives about the benefits and risks associated with upper limb OI prostheses.

Design: Patient perspective survey

Setting: Telephone administration

Participants: National sample of Veterans with upper limb loss.

Interventions: NA

Main Outcome Measures: Benefit-Risk survey developed for this study

Results: 28% of unilateral and 13% of bilateral amputees were willing to consider osseointegration surgery. Multivariate logistic regression models (OR; 95%CI) showed that transhumeral amputation level (OR 1.40; 1.01-1.98) was associated with greater willingness to consider surgery, while older age (OR 0.17; 0.09-0.32) and higher VR-12 MCS (OR 0.53; 0.35-0.81) were associated with less willingness. Having a durable/reliable device, the ability to do more activities, and having a comfortable device were rated as very important or somewhat important by 98% or more for every risk condition

Conclusions:

Persons who were older, had transradial amputation (compared to transhumeral), and those who had better mental functioning were less willing to consider this surgery. Respondents who were willing to consider surgery indicated that the most important potential benefits were obtaining a durable/reliable device, the ability to do more activities, and having a comfortable device. Most were willing to accept one or more risks of surgery, with long term risks including chronic pain, loss of nerve function or device failure, considered the most unacceptable.

Keywords: Prostheses; Osseointegration; Upper limb amputation; Patient perspectives

Introduction

Osseointegrated (OI) prostheses, which are attached to a residual limb by means of a fixture anchored in the bone, have a unique benefit-risk profile among prosthetic alternatives. They may improve user comfort, function, and sensation, but involve significant risks such as aseptic loosening (reported in 13-23% in upper extremity implants), periprosthetic fracture (reported in 0-18% of transfemoral implants, but 0% in upper extremity implants), intermedullary device breakage (reported in 27% of transradial implants) and infection (reported in 23-29%) [1, 2]. They have been marketed in Europe since the 1990's, in Australia since 2011, and in the U.S. under a Humanitarian Device Exemption since 2015. While lower-limb OI surgery is available in the US through the Humanitarian Device Exemption, upper-limb OI surgery has not yet been FDA approved in the U.S.. However, clinical trials of upper-limb OI surgery are ongoing. OI has been a treatment option for individuals with lower and upper limb loss in Europe for over 20 years . [3]

Evidence has grown about the potential benefits and risks associated with OI prostheses [2], and the trade-offs between OI and other prostheses make the choice to pursue an OI prosthesis a shared decision between patients and healthcare professionals. Information about the diversity of upper limb prosthesis user perspectives on these distinctive benefits and risks, prosthesis-user subpopulations for whom OI is most acceptable, and the outcomes that matter most to patients could help inform clinical and regulatory decision-making.

Recent 21st Century Cures legislation expanded the role of patient experience data in the FDA decision-making process, recognizing that the perspectives patients have about the impact of a condition and therapeutic options on their lives may be informative to regulators [4]. U.S. medical device approvals now include information about patient input considered during the

approval process, and the impact of OI prostheses on quality of life is increasingly a part of the conversation about decision-making related to clinical use of these devices [5-7]. To better understand prosthesis user perspectives about the benefits and risks associated with upper limb OI prostheses, we developed a patient perspective survey and administered it to a national sample of Veterans with upper limb loss.

Methods

Patient perspective survey development and pilot testing

All aspects of this study were approved by appropriate institutional review boards and all participants gave informed consent. Development of the patient perspective survey involved three stages: development of an initial item set, prioritization of the survey content, and cognitive and pilot testing. Each stage is shown in Fig 1. Detailed description of survey development is provided in Appendix A. Briefly, in Stage A, semi-structured interviews were conducted with seven participants to understand the desired improvements in prosthetic technology that might motivate persons to incur risks to obtain new devices, and an initial item set was developed. As described in a previous manuscript [7], this stage resulted in lists of challenges and limitations related to function and quality of life faced by the respondents and desired improvements in prosthetic technology. Preliminary items addressing potential benefits and risks were then drafted by one of the authors (HB).

In Stage B, participants with upper limb difference prioritized the lists of benefits and risks for inclusion in the survey. This stage involved a point allocation exercise to prioritize the potential benefit-risk considerations, followed by a focus group, and a survey reported elsewhere [8]. During the focus group, participants discussed challenges they had experienced with amputation or limb difference, what they liked and disliked about the prostheses they had used,

their experiences with pain, and what they would like to see in prostheses. Then they were asked to explain their responses to the prioritization exercise. Findings were used to refine items for inclusion in the benefit-risk survey. In Stage C, we tested potential participants' understanding of the item sets produced in Stage B and iteratively refined the items through cognitive testing and then pilot testing. Stage C resulted in the final version of the survey used in the national study. The final survey contained a yes/no screening question to ascertain participants' willingness to consider undergoing surgery to obtain a prosthesis that could restore sense of touch, provide more control over several types of prosthesis device movement, or eliminate the need for a prosthetic socket and harness, in addition to willingness to undergo specific risks associated with surgery. The benefit-risk items were only administered to those who answered yes to the screening question, indicating that they would consider undergoing surgery to obtain a particular benefit. The final version of the osseointegration survey section is shown in Appendix B. This manuscript reports on the data related to osseointegration. The results of benefit-risk questions about surgery to restore a sense of touch and provide more control over device movement will be reported elsewhere.

Recruitment

All Veterans with major upper limb amputation who received care in the VA between 2010-2016 (N=5639) were identified from VA Corporate Data Warehouse (CDW) sources. A total of 2288 persons were excluded (1479 deceased, and 601 missing valid addresses and/or phone numbers). Recruitment materials with opt out cards were sent to the remaining 3559 persons. Veterans who did not opt-out of participation (N=408) or inform us that they did not meet eligibility criteria (N=208) were contacted by telephone. Up to 10 phone call attempts were made. Veterans who were reached by phone (N=1893) were screened for eligibility.

Data Collection

Eight hundred eight persons completed all or part of the larger national interview survey. This survey, described elsewhere [9], contained questions related to demographics, amputation level, laterality and etiology, prosthesis use, as well as standardized measures including the VR-12 measure of health-related quality of life (HRQoL). The VR-12 is a Veteran version of the SF-12 Health Survey that produces the Physical Component Summary (PCS) (Cronbach alpha in this sample = 0.86) and the Mental Component Summary (MCS) (Cronbach alpha in this sample = 0.88) scores. [10, 11]

Data Analyses

We characterized demographics, amputation characteristics and prosthetic use for respondents. Descriptive analyses examined the proportion of respondents who indicated yes, no or not sure of their willingness to consider surgery for osseointegration by laterality of amputation (unilateral vs. bilateral), amputation level shoulder (SH), transhumeral (TH) and transradial (TR) gender, age group, category of HRQoL and etiology of amputation. We categorized HRQoL by separately grouping VR-12 PCS and MCS scores into three groups (low, medium, and high). The MCS and PCS have a population mean of 50 with a standard deviation (sd) of 10 (normative values). We considered those with scores more than 1 sd below the mean on each scale to have low scores on that scale, and those within 1 sd of the mean to have medium scores, and those with more than 1 sd above the mean to have high scores.

We collapsed the categories of yes and not sure of willingness to consider surgery for osseointegration and used chi-square tests to examine bivariate relationships between key patient related variables (age category, unilateral/bilateral amputation, amputation level, gender, laterality of amputation, etiology of amputation) and willingness to consider surgery. To examine

differences between sub-groups with three or more categories, we performed multiple comparison tests for variables using a Tukey-type method in SAS [12]. We then created a multivariate logistic regression model for willingness to consider surgery for osseointegration, including all variables that were significant in the bivariate analyses at $p < 0.10$.

For respondents who indicated a willingness (yes/unsure) to consider surgery, we examined ratings of importance of obtaining potential benefits (e.g. natural touch, better speed of movement control, ability to do more activities) given specific risks (e.g. overnight hospital stay, infection requiring antibiotics, infection requiring device removal). For respondents who indicated that they were willing to accept specific risks, we calculated the proportion who indicated that each of the specific benefits was important, somewhat important, or not important. We analyzed these data graphically to determine whether patterns of importance ratings varied by willingness to accept each type of risk.

We described the proportion of persons who were willing to accept each of the risks. We then compared ratings of benefit importance for each of the risks for prosthesis users and non-users, and by amputation level graphically and using Fisher's exact tests.

Results

Sampling frame and response rate-

Eight hundred eight (83%) of those screened to be eligible were successfully recruited into the study. The survey response rate and cooperation rate, calculated using the American Association for Public Opinion Research (AAPOR) methodology [13], was 47.7 % and 63.3%, respectively.

<Insert Fig 2. Flow Diagram>

Demographic, amputation-related and prosthetic use characteristics

The sample consisted of 776 unilateral amputees and 32 bilateral amputees (Table 2). Median age of the sample was 67.0 years (range 25 to 95); 764 (97.4%) were male and 20 (2.6%) were female. Table 1 shows characteristics of the sample. Seven hundred eighty-eight persons completed the entire interview, and 20 completed part but not the entire interview. Seventy-five percent of the sample identified as white, and 8.6% identified as Hispanic or Latino. Seventy percent of the sample were retired. Respondents had lost their limbs a median of 33.0 (range: 18.3 to 72.3) years prior to the interview. Amputation levels of respondents were 36.1% transradial (TR), 30.4% transhumeral (TH), 16.2% wrist joint (WD), 9.2% shoulder disarticulation (SD), 5.2% elbow disarticulation, and 3.0% forequarter amputation (FQ). Accident was the most common cause of amputation (62.1% unilateral, 62.5% bilateral), followed by “other” (54% unilateral, and 71.9% bilateral), and combat injury (35.5% unilateral, 28.1% bilateral). Burns were a prevalent cause of amputation for those with bilateral amputation (40.6%). Most respondents were current prosthesis users (60% unilateral, 84% bilateral respondents).

<Insert Table 1. Demographics characteristics of unilateral and bilateral amputee respondents>

Willingness to Undergo Surgery

Table 2 shows the proportion of respondents who indicated willingness to consider osseointegration surgery by sub-group characteristics. We found that 28.2% of unilateral and

12.9% of bilateral amputees were willing to consider osseointegration surgery, and 13.4% of unilateral and 12.9% of bilateral amputees were unsure.

<Insert Table 2. Proportion of participants willing to consider osseointegration surgery >

By amputation level, persons with TH amputation were the sub-group most likely to consider osseointegration surgery (35.0% yes, 10.9% unsure). A smaller proportion of respondents who had lost their limbs due to combat injury, and a greater proportion of those who had lost their limbs due to accident indicated a willingness to undergo osseointegration surgery compared to persons with amputation from other etiologies.

Results of the bivariate analyses comparing participant characteristics associated with willingness to undergo surgery (yes or unsure vs. no) for each of the major benefits are shown in Table 3. Younger age, MCS category, and non-combat amputation were statistically associated with willingness to undergo osseointegration surgery. Post-hoc analyses revealed that there were statistically significant differences between the high and low and high and medium categories for MCS, with those with the highest category (best mental HrQoL) being less likely to be willing to consider surgery for osseointegration (results not shown). Post-hoc analyses by amputation level did not show any statistically significant differences by level (results not shown).

<Insert Table 3 Bivariate comparisons of characteristics of participants by willingness to consider osseointegration>

Multivariate logistic regression models that included all variables statistically significant at $p \leq 0.10$ showed that age, amputation levels, and MCS were independently associated with willingness to consider surgery (Table 4). Specifically, the odds of being willing to consider

surgery were 0.17 times lower for those 75 and older compared to those 18-45 years. Relative to those with unilateral transradial level amputation, the odds of being willing to consider surgery were 1.40 higher for persons with unilateral transhumeral level amputation and 0.50 lower for those with bilateral amputation.

<Insert Table 4. Multivariable logistic regressions for willingness to undergo surgery>

Table 5 shows the proportion of respondents willing to accept each specific risk among those who were definitely or maybe willing to consider osseointegration surgery. Overall, long term risks, such as chronic pain, loss of some nerve function, or device failure requiring it to be removed, were unacceptable to the greatest proportion of respondents (21.7%). Short-term restrictions on movement as well as pain and weakness for about a month were unacceptable to the smallest proportion (2.5%). Forty-seven percent of respondents were willing and 40% were maybe willing to risk a serious infection that would require antibiotics.

<Insert Table 5. Proportion of respondents willing to accept each surgical risk condition >

Importance ratings of benefit factors were very similar across risk types. All potential benefits were considered very important or somewhat important for each risk condition by the majority of respondents. Having a durable/reliable device, the ability to do more activities, and having a comfortable device were rated as very important or somewhat important by 98% or more respondents for every risk condition. In contrast, naturalness of touch and water-resistance were the benefits rated not at all important by the greatest proportion of respondents (7.3-8.1% and 4.2-5.5% respectively). As an example, Fig 3 shows the importance ratings of each potential

benefit, given the risk of incurring an infection requiring IV antibiotics and hospitalization.

Importance rating for all other risks are shown in Appendix C.

< Insert Fig 3 Ratings of importance of possible benefit for persons willing to risk infection requiring IV and Hospitalization>

Comparison of importance ratings for each potential benefit-risk combination by amputation level showed differences at $p < 0.05$ for several benefits. We observed several statistically significant differences in importance rankings by amputation level. Although there were small differences in statistically significant findings, there was good consistency of findings across benefit-risk combinations by amputation level (Appendix C). As an example, for the risk of willingness to incur infection requiring IV antibiotics and an overnight hospital stay (Fig 4), there were differences in group rankings for the importance of more activities and durability/reliability of the device. The smallest proportion of persons with shoulder level amputation rated the ability to do more activities as very important. Although not statistically significantly different by sub-group in any risk condition, we also found that 100% of bilateral amputees rated water and dirt resistance and ability to lift more than 20 lbs. as very important in willingness to incur risk, and nearly 100% rated durability and reliability as very important. In contrast, the naturalness of touch was the benefit rated not at all important by the greatest proportion of respondents across all amputation levels in most every risk condition.

< Insert Fig 4. Sub-group comparisons of importance of factors for those who were willing to risk infection requiring antibiotics to obtain an osseointegrated prosthesis by amputation level>

Comparisons of importance ratings for each potential benefit-risk combination by current prosthetic use did not show statistical differences except for the benefit of water/dirt resistance among those willing to consider long-term risks of pain or weakness during recovery (Appendix C). In these two comparisons, water/dirt resistance was more important to prosthetic users than to nonusers ($p<0.05$).

DISCUSSION

We conducted a first-of-its-kind national study that assessed upper limb amputee's willingness to consider osseointegration surgery. Our survey, limited to Veterans, also evaluated the importance of receiving specific benefits and examined whether these importance rankings varied by amputation level and for unilateral and bilateral amputees. Our survey demonstrates that amongst Veterans, there are a substantial proportion who would consider OI surgery should it be available. Our specific findings highlight those risks that are considered most and least acceptable, as well as the benefits most desired. This information is informative to researchers recruiting participants to OI trials and to clinicians who discuss the risks and benefits of OI with their patients. We found that 28% of unilateral and 13% of bilateral amputees were willing to consider osseointegration surgery, while a substantial proportion (approximately 13%) were unsure. A greater proportion of respondents who were in older age categories, had bilateral amputation, and had better mental health functioning answered that they would not consider surgery. We found that persons with transhumeral amputation, a group with high abandonment rates [14], who may have difficulties with prosthesis socket fit, and thus are likely to receive the greatest benefit, were most likely to say they would consider this surgery (35%).

Our findings mirror those reported by Engdahl et al., who surveyed upper limb amputees about their interest in novel prosthetic interfaces but did not explicitly study osseointegration. They found that younger participants and those with unilateral amputation were more likely to be interested in the three invasive interfaces that they studied [15].

For those who indicated that they were or might be willing to consider osseointegration surgery, we examined whether ratings of benefit importance varied by specific risk conditions. The benefits that were rated least important across risks included natural touch, water/dirt resistant, and ability to lift more than 20 lbs. We found remarkable consistency in the ratings of benefits that were important across risks, with all potential benefits considered very important or somewhat important by most participants. This finding is not surprising because the list of potential benefits in our survey was identified through formative research with persons with amputation and other stakeholders.

Our study also quantified the acceptability of incurring a variety of post-surgical risks among those who indicated an openness to considering osseointegration surgery. All risks were acceptable or possibly acceptable to the majority of respondents who were willing or might be willing to consider osseointegration surgery. This demonstrates that persons who are open to considering surgery at all are willing to risk some adversity. Our results help sort these post-surgical risks by their perceived severity, with short term risks and 6 months of physical therapy the most acceptable and risk of bone breaking and long-term risks (including chronic pain, loss of some nerve function, or device failure requiring it to be removed) the most unacceptable. The risk of a serious infection that would require antibiotics was not a deterrent to most participants, with 87% of respondents willing or maybe willing to accept this risk.

We found that ratings of benefit importance were consistent across all risk categories, but that persons with bilateral and shoulder level amputation, who are arguably more functionally impaired, weighed the importance of potential benefits directly related to function differently. Virtually all persons with bilateral amputation indicated that durability, water resistance, and lifting >20 lbs. were very important. In comparison, a greater proportion of persons with above and below elbow level amputation indicated that more activities and comfortable fit were very important.

We observed that persons categorized as having poor mental health were more likely to be willing to consider surgery for osseointegration. Further study is needed to disentangle the relationship between mental health and willingness or unwillingness to consider osseointegration surgery. We hypothesize that persons with poor prosthesis fit or who are uncomfortable about the appearance of their prosthesis may have poorer mental health and may be more open to considering interventions that can remediate their condition.

Limitations:

Our study had several limitations. First, it is possible that some participants did not fully understand what osseointegration surgery was. We did provide a brief explanation of osseointegration surgery, but we did not assess whether participants were familiar with this surgery or not, and we did not assess comprehension after the explanation was provided. Some may not have fully understood what the surgery entailed or appreciated how osseointegration would be used to attach the prosthesis. While osseointegration has been available in Europe for decades, most US amputees have not been exposed to this technology, and it is unlikely that they have ever met a person who had an osseointegrated limb.

Another limitation is that our sample included only Veterans who had received care at VA Medical Centers. These participants may not represent the larger population of Veterans or of US upper limb amputees more generally. However, we sampled 100% of Veterans who met our eligibility criteria and had a strong response rate, and thus our findings are likely

generalizable to Veterans with upper limb amputation receiving healthcare at the VA. We believe that the findings are generalizable to both male and female Veterans. Although the Veteran sample is predominantly male, the response rate for females was high (62.8% female, vs 47.3% male). However, given the small number of females in the sample overall, there are limitations for generalizing from our findings of female Veterans to the civilian population..

Lastly, although we conducted statistical comparisons of importance for specific risk conditions, our analyses were limited due to small sample sizes for shoulder level and bilateral amputees, which may have resulted in insufficient power to detect small differences. Further research with larger samples and non-Veterans is needed to confirm or refute our findings.

Conclusions

We conducted a national survey of Veterans with major upper limb loss to assess their willingness to consider osseointegration and to understand their perspectives on osseointegration's potential benefits and risks. Twenty-eight percent of respondents were willing to consider osseointegration surgery. Persons who were older, had transradial amputation (compared to transhumeral), and those who had better mental functioning were less willing to consider this surgery. Respondents who were willing to consider surgery indicated that the most important potential benefits were having a durable/reliable device, the ability to do more activities, and having a comfortable device. Most were willing to accept one or more risks of surgery, with long term risks including chronic pain, loss of nerve function or device failure, considered the most unacceptable.

References

1. Potter BK. From Bench to Bedside: A Perfect Fit? Osseointegration Can Improve Function for Patients with Amputations. *Clin Orthop Relat Res*. 2016;474(1):35-7.
2. Atallah R, Leijendekkers RA, Hoogeboom TJ, Frolke JP. Complications of bone-anchored prostheses for individuals with an extremity amputation: A systematic review. *PLoS One*. 2018;13(8):e0201821.
3. Tillander J, Hagberg K, Hagberg L, Branemark R. Osseointegrated titanium implants for limb prostheses attachments: infectious complications. *Clin Orthop Relat Res*. 2010;468(10):2781-8.
4. Wilson H, Anatchkova M, Gelhorn H. A Perspective on the 21ST Century Cures Act: Patient-Focused Drug Development. 2017 [cited November]; 1-4]. Available from: https://www.evidera.com/wp-content/uploads/2017/11/04-A-Perspective-on-The-21st-Century-Cures-Act-Patient-Focused-Drug-Development_2017Nov-1.pdf.
5. Khemka A, Frossard L, Lord S, Bosley B, Muderis A, editors. Health-related quality of life of individuals with transfemoral amputation fitted with the Transcutaneous Bone Anchoring Prosthesis following the OGAAP. 6th International Conference Advances in Orthopaedic Osseointegration; 2015 March 26-27; Las Vegas, NV.
6. Hagberg K, Hansson E, Branemark R. Outcome of percutaneous osseointegrated prostheses for patients with unilateral transfemoral amputation at two-year follow-up. *Arch Phys Med Rehabil*. 2014;95(11):2120-7. Epub 2014/07/30.
7. Hansson E, Hagberg K, Cawson M, Brodtkorb TH. Patients with unilateral transfemoral amputation treated with a percutaneous osseointegrated prosthesis. *The bone & joint journal*. 2018;100-B(4):527-34.
8. Janssen EM, Benz HL, Tsai JH, Bridges JF. Identifying and prioritizing concerns associated with prosthetic devices for use in a benefit-risk assessment: a mixed-methods approach. *Expert review of medical devices*. 2018;15(5):385-98.
9. Resnik L, Ekerholm, S, Borgia, M, Clark, M. A National Study of Veterans with major upper limb amputation: Survey methods, participants, and summary findings. Under Review.
10. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-33.
11. Ware JE, Jr. SF-36 health survey update. *Spine*. 2000;25(24):3130-9. Epub 2000/12/22.
12. Elliot AC, Reisch JS. Implementing a Multiple Comparison Test for Proportions in a 2xc Crosstabulation in SAS®. Center for Biostatistics and Clinical Science: UT Southwestern Medical Center, Dallas; Available from: <http://www2.sas.com/proceedings/sugi31/204-31.pdf>.

13. Research. AAFPO. Response Rates - An Overview. 2018; Available from: <https://www.aapor.org/Education-Resources/For-Researchers/Poll-Survey-FAQ/Response-Rates-An-Overview.aspx>.
14. Biddiss EA, Chau TT. Upper limb prosthesis use and abandonment: a survey of the last 25 years. *Prosthet Orthot Int*. 2007;31(3):236-57.
15. Engdahl SM, Chestek CA, Kelly B, Davis A, Gates DH. Factors associated with interest in novel interfaces for upper limb prosthesis control. *PLoS One*. 2017;12(8):e0182482.

	Unilateral Amputees N=776	Bilateral Amputees N=32	All N=808
	Median (range)	Median (range)	Median (range)
Age (Years)	67.0 (25.0, 93.0)	67.0 (33.0, 95.0)	67.0 (25.0, 95.0)
Missing (n)	n=24	n=0	n=24
Years since initial amputation (either side)	33.1 (1.3, 73.6)	31.2 (5.4, 72.3)	33.0 (1.3, 73.6)
Years since amputation (second side)	NA	29.8 (5.4, 72.3)	NA
Missing (n)	n=21	n=0	n=21
	N (%)	N (%)	N (%)
Age category			
18,45	99 (13.2)	5 (15.6)	104 (13.3)
45,65	207 (27.5)	9 (28.1)	216 (27.6)
65,75	340 (45.2)	13 (40.6)	353 (45.0)
75+	106 (14.1)	5 (15.6)	111 (14.2)
Missing (n)	n=24	n=0	n=24
Gender			
Male	755 (97.3)	32 (100.0)	787 (97.4)
Female	21 (2.7)	0 (0.0)	21 (2.6)
Missing (n)	n=0	n=0	n=0
Race			
White	583 (77.5)	22 (68.8)	605 (74.9)
Black	86 (11.4)	3 (9.4)	89 (11.0)
Native American	5 (0.7)	0 (0.0)	5 (0.6)
Other (including mixed race)	30 (4.0)	4 (12.5)	34 (4.2)
Unknown	48 (6.4)	3 (9.4)	75 (9.3)
Missing (n)	n=24	n=0	n=24
Hispanic or Latino			
Yes	62 (8.2)	5 (15.6)	67 (8.6)
No	678 (90.2)	26 (81.3)	704 (89.8)
Unknown	12 (1.6)	1 (3.1)	13 (1.7)
Missing (n)	n=24	n=0	n=24
Employment			
Employed full-time	73 (9.7)	1 (3.1)	74 (9.4)
Employed part-time	31 (4.1)	13 (40.6)	31 (4.0)
Student	20 (2.7)	0 (0.0)	20 (2.6)

Retired, but employed after amputation	373 (49.6)	13 (40.6)	386 (49.2)
Retired, but not employed after amputation	152 (20.2)	5 (15.6)	165 (21.1)
On medical leave	9 (1.2)	0 (0.0)	9 (1.2)
Other	93 (12.4)	0 (0.0)	98 (12.5)
Unknown	1 (0.1)	0 (0.0)	1 (0.1)
Missing (n)	n=24	n=0	n=24
Laterality of amputation			
Unilateral Right	370 (47.7)	0 (0.0)	370 (45.8)
Unilateral left	406 (52.3)	0 (0.0)	406 (50.3)
Bilateral	0 (0.0)	32 (100.)	32 (4.0)
Missing (n)	n=0	n=0	n=0
Amputation Level			
Forequarter	23 (3.0)	1 (3.1)	0 (0.0)
At the shoulder joint	71 (9.2)	1 (3.1)	1 (3.1)
Above the elbow	236 (30.4)	5 (15.6)	4 (12.5)
At the elbow	40 (5.2)	14 (43.8)	1 (3.1)
Below the elbow	280 (36.1)	10 (31.3)	20 (62.5)
At the wrist joint	126 (16.2)	0 (0.0)	6 (18.8)
Through the hand	0 (0.0)	1 (3.1)	0 (0.0)
Missing (n)	n=0	n=0	
Etiology of amputation			
Combat injury	275 (35.5)	9 (28.1)	9 (28.1)
Accident	481 (62.1)	20 (62.5)	20 (62.5)
Burn	81 (10.5)	13 (40.6)	13 (40.6)
Cancer	30 (3.9)	0 (0.0)	0 (0.0)
Diabetes	11 (1.4)	0 (0.0)	1 (3.1)
Infection	86 (11.1)	9 (28.1)	8 (25.0)
Other	417 (54.0)	21 (65.6)	23 (71.9)
Missing (n)	n=0 to 3	n=0	n=0

Table 1. Characteristics of unilateral and bilateral amputee respondents

		Willing to consider osseointegration?		
	N	Yes (N=215)	No (N=461)	Not Sure (N=104)
Laterality				
Unilateral	776	211 (28.2)	438 (58.5)	100 (13.4)
Bilateral	32	4 (12.9)	23 (74.2)	4 (12.9)
Amputation Level				
Unilateral SH [‡]	94	25 (27.5)	521(56.0)	15 (16.5)
Unilateral TH [†]	276	93 (35.0)	144 (54.1)	29 (10.9)
Unilateral TR [‡]	406	93 (23.7)	243 (62.0)	56 (14.3)
Bilateral amputation	32	4 (12.9)	23 (74.2)	4 (12.9)
Ever used prosthesis				
Yes	749	202 (94.0)	431 (93.5)	95 (91.4)
No	52	12 (5.6)	29 (6.3)	9 (8.7)
Unknown	2	1 (0.5)	1 (0.2)	0 (0.0)
Current prosthesis user				
Yes	490	120 (59.4)	290 (67.8)	63 (66.3)
No	254	82 (40.6)	136 (31.8)	32 (33.7)
Unknown	2	0 (0.0)	2 (0.5)	0 (0.0)
Ever used prosthesis				
Yes	749	202 (94.4)	431 (93.7)	95 (91.4)
No	52	12 (5.6)	29 (6.3)	9 (8.7)
Gender				
Male	764	208 (96.7)	450 (97.6)	102 (98.1)
Female	20	7 (35.0)	11 (55.0)	2 (10.0)
Age				
18,45	104	41 (39.4)	45 (43.3)	18 (17.3)
45,65	216	71 (32.9)	108 (50.0)	37 (17.1)
65,75	353	87 (24.8)	220 (62.7)	44 (12.5)
75+	111	16 (14.7)	88 (80.7)	5 (4.6)
PCS[§]				
Low	234	68 (29.4)	131 (56.7)	32 (13.9)
Medium	511	136 (26.7)	304 (59.7)	69 (13.6)
High	13	3 (23.1)	10 (76.9)	0 (0.0)
MCS[¶]				
Low	188	60 (31.9)	96 (51.1)	32 (17.0)
Medium	344	100 (29.3)	196 (57.5)	45 (13.2)
High	226	47 (21.0)	153 (68.3)	24 (10.7)
Etiology of amputation				
Combat injury				
Yes	284	61 (22.3)	176 (64.2)	37 (13.5)
No	523	154 (30.4)	285 (56.3)	67 (13.2)
Accident				

	Yes	501	137 (28.1)	280 (57.5)	70 (14.4)
	No	305	78 (26.6)	181 (61.8)	34 (11.6)
Burn					
	Yes	94	17 (19.3)	57 (64.8)	14 (15.9)
	No	711	198 (28.6)	404 (58.4)	90 (13.0)
Cancer					
	Yes	30	8 (28.6)	18 (64.3)	2 (7.1)
	No	776	207 (27.5)	443 (58.9)	102 (13.6)
Diabetes					
	Yes	12	6 (50.0)	5 (41.7)	1 (8.3)
	No	792	209 (27.2)	456 (59.4)	103 (13.4)
Infection					
	Yes	95	29 (31.5)	48 (52.2)	15 (16.3)
	No	709	186 (27.0)	413 (60.0)	89 (12.9)
Other					
	Yes	440	116 (27.0)	250 (58.3)	63 (14.7)
	No	365	99 (28.2)	211 (60.1)	41 (11.7)

Table 2. Proportion of participants willing to consider osseointegration

‡ SH=Shoulder disarticulation or forequarter

† TH=Transhumeral

‡ TR=Transradial

§ PCS=Physical Component Summary of the VR-12 Health Survey

¶ MCS=Mental Component Summary of the VR-12 Health Survey

	N	Yes /Maybe (N=319)	No (N=461)	Chisq/Fisher's Exact p
Amputation Level				0.062
Unilateral SH	94	40 (44.0)	51 (56.5)	
Unilateral TH	276	122 (45.9)	144 (54.1)	
Unilateral TR	406	149 (38.0)	243 (62.0)	
Bilateral amputation	32	8 (25.8)	23 (74.2)	
Laterality				0.081
Unilateral	776	311 (41.5)	438 (58.5)	
Bilateral	32	8 (25.8)	23 (74.2)	
Ever used prosthesis				0.943
Yes	749	297 (93.1)	431 (93.5)	
No	52	21 (6.6)	29 (6.3)	
Missing	2	1 (0.3)	1 (0.2)	
Current prosthesis user				0.080
Yes	490	183 (61.6)	200 (67.8)	
No	254	114 (36.4)	136 (31.8)	
Missing	2	0 (0.0)	2 (0.5)	
Gender				0.705
Male	764	310 (40.8)	450 (97.6)	
Female	20	9 (45.0)	11 (55.0)	
Age				<0.001
18,45	104	59 (56.7)	45 (43.3)	
45,65	216	108 (50.0)	108 (50.0)	
65,75	353	131 (37.3)	220 (62.7)	
75+	111	21 (19.3)	88 (80.7)	
PCS				0.311
Low	234	100 (43.3)	131 (56.7)	
Medium	511	205 (40.3)	304 (59.7)	
High	13	3 (23.1)	10 (76.9)	
MCS				0.001
Low	188	92 (48.9)	96 (51.1)	
Medium	344	145 (42.5)	196 (57.5)	
High	226	71 (31.7)	153 (68.3)	
Etiology of amputation				
Combat injury				0.032
Yes	284	98 (35.8)	176 (64.2)	
No	523	221 (43.7)	285 (56.3)	
Accident				0.239
Yes	501	207 (42.5)	280 (57.5)	
No	305	112 (38.2)	181 (61.8)	
Burn				0.251

	Yes	94	31 (35.2)	57 (64.8)	
	No	711	288 (41.6)	403 (58.3)	
Cancer					0.570
	Yes	30	10 (35.7)	18 (64.3)	
	No	776	309 (41.1)	443 (58.9)	
Diabetes					0.246
	Yes	12	7 (58.3)	5 (41.7)	
	No	792	312 (40.6)	455 (59.3)	
Infection					0.150
	Yes	95	44 (47.8)	48 (52.2)	
	No	709	275 (40.0)	413 (60.1)	
Other					0.603
	Yes	440	179 (41.7)	250 (58.3)	
	No	365	140 (39.9)	211 (60.1)	

Table 3. Bivariate comparisons of characteristics of participants by willingness to consider osseointegration

‡ SH=Shoulder disarticulation or forequarter

† TH=Transhumeral

‡ TR=Transradial

§ PCS=Physical Component Summary of the VR-12 Health Survey

¶ MCS=Mental Component Summary of the VR-12 Health Survey

		Osseointegration (N=753)	
		OR (95% CI)	p
Amputation Level			
	Unilateral SH	1.19 (0.73-1.95)	0.488
	Unilateral TH	1.40 (1.00-1.97)	0.0050
	Unilateral TR	(ref)	
	Bilateral amputation	0.50 (0.21-1.20)	0.118
Age			
	18,45	(ref)	
	45,65	0.57 (0.34-0.96)	0.033
	65,75	0.40 (0.25-0.64)	<0.001
	75+	0.17 (0.09-0.32)	<0.001
MCS			
	Low	(ref)	
	Medium	0.86 (0.59-1.24)	0.414
	High	0.53 (0.35-0.81)	0.003
Etiology of amputation			
Combat injury			
	Yes	0.68 (0.44-1.07)	0.093
	No	(ref)	
Accident			
	Yes	1.01 (0.67-1.54)	0.952
	No	(ref)	
Infection			
	Yes	1.32 (0.82-2.12)	0.256
	No	(ref)	

Table 4. Multivariable logistic regressions predicting willingness to consider osseointegration

OR=Odds Ratio

‡ SH=Shoulder disarticulation or forequarter

† TH=Transhumeral

‡ TR=Transradial

¶ MCS=Mental Component Summary of the VR-12 Health Survey

	N=319		
	Yes	Maybe	No
Risk condition	N (%)	N (%)	N (%)
Risk of infection that would require antibiotics	149 (47.2)	126 (39.9)	41 (13.0)
Risk of serious infection that would require removing the device	186 (58.5)	96 (30.2)	36 (11.3)
Risk of bone breaking that would require surgery to remove the device	162 (50.9)	97 (30.5)	59 (18.6)
Long-term risks	163 (51.9)	83 (26.4)	68 (21.7)
Pain or weakness during the recovery from surgery of about 1 month	250 (78.9)	53 (16.7)	14 (4.4)
Short-term restrictions on movement and exercise for up to 1 month	258 (81.4)	51 (16.1)	8 (2.5)
Up to 6 months of physical therapy	261 (82.3)	47 (14.8)	9 (2.8)

Table 5. Willingness to accept each surgical risk condition among those definitely or maybe willing to undergo osseointegration surgery

Figure 1. Stages of Benefit-Risk Survey Development

Figure 2. Flow Diagram

Figure 3. Benefit factor ratings for those who would consider Osseointegration surgery (yes/maybe): Example figure using those willing to risk infection requiring IV antibiotics and hospitalization)

Fig 4. Sub-group comparisons of importance of factors for those who were willing to risks infection requiring antibiotics in order to obtain an osseointegrated prosthesis by amputation level

*significant at $p < 0.05$

FQ=Forequarter