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**TITLE:** Psychosocial Predictors in VCA

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# REPORT DOCUMENTATION PAGE

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<b>14. ABSTRACT</b> During year one, compilation of the International Registry of Hand and Composite Tissue Transplantation (IRHCTT) and psychosocial surveys was performed. Focus group interviews of transplant recipients, social support and experts in the field were completed and transcribed. During year two, data analysis from the IRHCTT and psychosocial surveys identified 5 factors associated with transplant outcomes and perceived success. The factors were tested in a vignette survey distributed to 100 participants. Analysis determines that increased number of negative factors leads to worse perceived outcomes. During year three qualitative thematic analysis was performed for the focus group interviews with several themes being associated with perceived success. Three papers have been published with a fourth paper being submitted. A mirroring focus group study has been approved for subaward in Innsbruck, Austria. All focus group interviews have been performed and qualitative analysis is underway.					
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## 1. INTRODUCTION:

Over the past 15 years, upper extremity vascularized composite allotransplantation (VCA) has moved from a purely experimental option for a few amputees to, at some institutions, the standard of care. This transition has occurred without a detailed, comprehensive, or objective analysis of the psychosocial factors that contribute to the success or failure of these unique transplants. The selection of transplant candidacy is currently an inherently subjective process. This research sought to determine psychosocial factors associated with perceived success in upper extremity vascularized composite allotransplantation.

During the first year, data from the International Registry of Hand and Composite Tissue Transplantation (IRHCTT) was compiled. Limited psychosocial data existed within the IRHCTT database and a psychosocial survey was performed and distributed to centers within the Registry. Focus group interviews of transplant recipients, their social support and transplantation experts were performed and transcribed.

During year two, data analysis from the IRHCTT and psychosocial surveys identified 5 factors associated with transplant outcomes and perceived success. The factors were tested in a vignette survey distributed to 100 global participants. Analysis determined that increased number of negative factors leads to worse perceived outcomes.

During year three, qualitative thematic analysis was performed for the focus group interviews with several themes being associated with perceived success. Three papers have been published with a fourth paper being submitted. A mirroring focus group study has been approved for subaward with the Medical University of Innsbruck, Austria. All focus group interviews have been performed and qualitative analysis is underway. A comparison paper between the Innsbruck versus Boston data will be written and submitted based on the findings.

By aggregating the quantitative data available with the IRHCTT, obtaining qualitative data from patients and physicians internationally, and combining the opinions of global experts through vignettes, we have identified psychosocial factors associated with perceived success in upper extremity transplants. These associated factors may be predictive of outcomes in patients who have been transplanted and may be modified in those who will be transplanted going forward.

**2. KEYWORDS:**

Vascularized Composite Allotransplantation (VCA)  
 Psychosocial factors  
 Qualitative data  
 Focus group

**3. ACCOMPLISHMENTS:**

**What were the major goals of the project?**

The major goals of this project as stated in the Statement of Work include:		
<u>Specific Aim 1</u> – To collate the comprehensive array of demographic, anatomic, medical, immunologic, social, psychiatric, donor and surgical/logistic variables held in the International Registry of Hand and Composite Tissue Transplantation (includes almost all cases performed to date internationally) and undertake statistical analysis.	Timeline in months per SOW	Completion
1. Hire staff including coordinator	1-3	
2. Contact and coordinate with all sites	1-3	
3. Finalize IRB documents	3	
<i>Milestone: All necessary staff hired</i>	3	8/2017
<i>Milestone: IRB approval at BWH</i>	6	8/2017
4. Submit HRPO documents	1-3	
<i>Milestone: HRPO approval</i>	6	8/2017
5. Develop online databases	3-6	
6. Test data collection and storage systems	3-6	
<i>Milestone: Databases online and functional</i>	6	1/2018
7. Review of patients in IRHCTT database and collation of data	6-9	
8. Detailed review with collection of additional data from individual centers	6-12	
<i>Milestone: Data available online</i>	12	1/2018
9. Descriptive statistical analysis	12-24	
<i>Milestone: Detailed descriptive statistics complete and available</i>	24	3/2019
<u>Specific Aim 2</u> – To elucidate the core factors involved in transplant success and failure utilizing qualitative research methods to guide selection of patients.	Timeline in months per SOW	Completion
1. Review of available data regarding key variables	6-12	
2. Focus groups and in-depth interviews with patients, social support, and expert clinicians to gather qualitative data	6-12	
3. Collection of data and preliminary analysis	12-18	
4. Review with statistician	18	
<i>Milestone: Compilation of comprehensive set of potential transplant outcome predictors</i>	18	6/2019

Specific Aim 3 – To develop a model, utilization expert opinion of hypothetical patients with a variety of psychosocial variables and the RAND/UCLA appropriateness method, to help objectify the evaluations of hand transplant patients and validate the model developed in Aims 1 and 2 in actual patients from the several large volume centers where complete data is available.	Timeline in months per SOW	Completion
1. Collection of clinical experts through transplant meetings	6-12	
<i>Milestone: Commitment from clinical experts</i>	6-12	11/2018
2. Development and review of survey	12-18	
3. Review with statistician	12-18	
<i>Milestone: Survey useable</i>	12-24	10/2018
4. Mailing and contact list developed	6-12	
5. Survey deployed	12-18	
6. Follow up with survey recipients	18-24	
<i>Milestone: Survey completed</i>	24	12/2018
7. Tabulation of data	24-27	
<i>Milestone: Data available for analysis</i>	27	12/2018
8. Statistical model developed	27-33	
<i>Milestone: Model complete</i>	33	3/2019
9. Database population with all available data to date	33-36	
<i>Milestone: Data available</i>	36	8/2020
10. Each patient score determined	36	
11. Each outcome measure determined	33-36	
12. Correlation of variables with outcome	33-36	
<i>Milestone: Study validation</i>	36	5/2021

### What was accomplished under these goals?

Over the past 15 years, upper extremity vascularized composite allotransplantation (VCA) has moved from a purely experimental option for a few amputees to the standard of care at certain institutions. This transition has occurred without a detailed, comprehensive, or objective analysis of the psychosocial factors that contribute to the success or failure of these unique transplants. The selection of transplant candidacy is currently an inherently subjective process. This research sought to determine psychosocial factors associated with perceived success in upper extremity VCA.

This study was divided into three aims:

1. Review of the global data through collaboration with the International Registry of Composite Tissue Transplantation (IRHCTT) and development of a psychosocial survey
2. Focus group interviews of VCA recipients, their support person and experts in the field.
3. Development of a model to demonstrate psychosocial risk for VCA candidates based on expert opinion.

Upon initiation of the study, IRB and HRPO approvals were submitted and obtained for each of the three specific aims of this study. Through collaboration with the IRHCTT, deidentified data from 1998 to 2016, collated from 19 centers around the globe was shared and analyzed for 62 VCA recipients (36 bilateral and 26 unilateral recipients). Data included factors pertaining to demographics; anatomy (level of amputation, transplant performed); graft status; medical, immunological (tissue matching, immunosuppression), surgical (ischemia time, vessels/nerve coapted), and rejection status; and social factors for transplant donors and recipients. Psychosocial factors were limited to alcohol, nicotine, and drug use, and an unstandardized perceived level of satisfaction.

A supplementary psychosocial survey was developed based on aggregation of solid-organ transplant candidacy assessment instruments: the “Psychosocial Assessment of Candidates for Transplantation”, the “Transplant Evaluation Rating Scale”, and the “Stanford Integrated Psychosocial Assessment for Transplantation” which emphasized the importance of psychiatric history, family support, substance dependency history, knowledge of transplantation, and history of compliance. The psychosocial survey focused on themes of depression, post-traumatic stress disorder (PTSD), anxiety, interpersonal functioning and dependence, compliance (including medication compliance, punctuality, and participation in therapy), chronic pain, social support, quality of life, and patient expectations. Analysis was focused on the four prospectively collected variables from the IRHCTT and 19 psychosocial risk factors from the survey.

The psychosocial survey was distributed to the 19 global transplant centers and completed by the center’s lead clinician, psychiatrist, or their designee. Of these, 43 surveys (69%) were retrospectively completed. Survey responses were scored between 1 and 5, with 1 being the least favorable answer and 5 being the most favorable, suggesting that transplant recipients with a wide range of psychosocial variables have been transplanted. 38 recipients (88%) had intact transplant(s) and 5 (12%) had their transplant(s) amputated.

In total, 29 of 43 recipients (67%) were reported to have anxiety and 5 underwent transplant removal (17%). No recipients without anxiety (N=14, 33%) reported transplant loss. One-third reported having and being treated for depression (N=14, 33%) with minimally higher risk of transplant removal compared to those without depression (N=29, 67%) with the difference well below statistical significance (14% versus 10%;  $p = 0.17$ ). Among recipients with PTSD (N=18, 42%), 4 recipients (22%) had their transplant(s) removed; among non-PTSD transplant recipients (N=25, 58%) only 1 subject (4%) underwent removal ( $p = 0.02$ ). There was a negative association between participation in occupational therapy (OT) and transplant removal. While most actively engaged in OT and home exercises (N = 28, 65%), recipients who did not (N = 15, 35%) had a nearly 3-fold risk of transplant. This difference did not reach statistical significance (20% versus 7%;  $P = 0.09$ ). Recipients who were not “always on time” for OT (N = 19, 44%) also had double the risk of transplant removal compared with recipients who were “always on time” for OT (N = 24, 55%), although again this did not reach statistical significance (16% versus 8%;  $P = 0.29$ ). Most UET recipients in our study were felt to have realistic expectations toward posttransplant function. Recipients’ expectations toward posttransplant function show a strong association with transplant status. Among recipients felt to have realistic expectations of postsurgical function (N = 34, 79%), 2 recipients (6%) lost their transplants, compared with 3 recipients (33%) who did not have realistic expectations (N = 9, 21%;  $P = 0.05$ ). The majority of

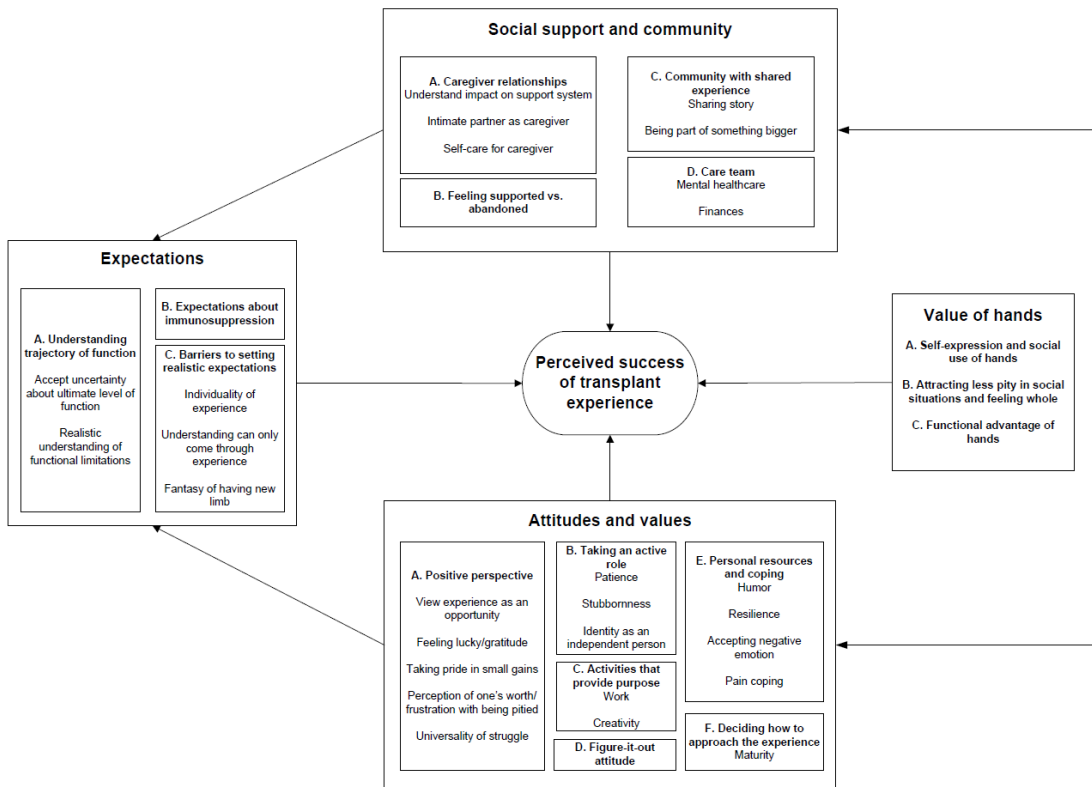
UET recipients had good or very involved family/friend support at the time of survey completion (N = 33, 77%). Recipients with strong support had a lower chance of transplant removal compared with recipients with poor or fair support (N = 10, 23%), but the difference did not reach statistical significance (6% versus 30%; P = 0.14).

Anxiety, depression, PTSD, participation in occupational therapy (OT), expectations for post-transplant function, and social support were associated with postsurgical transplant status, among which anxiety, PTSD, and post-transplant expectations reached statistical significance. This concluded aim 1 and all major goals were met. A manuscript describing our quantitative work was published in 2020 in *Plastic Reconstructive Surgery Global Open* (Plast Reconstr Surg Glob Open 2020;8:e3133; doi: 10.1097/GOX.0000000000003133).

For the second aim, qualitative work was initiated to understand the psychosocial factors associated with perceived success in upper extremity VCA. Four upper extremity VCA recipients, 3 primary caregivers and 13 experts in the field of transplantation were interviewed in focus groups by a psychiatrist and psychologist. Expert participants included 4 transplant surgeons, 2 transplant physicians, 2 nurses, 1 social worker, 3 occupational therapists, and 1 research administrator. Semi-structured face-to-face focus group interviews were conducted using an interview guide created through collaboration among the transplant surgery team, psychiatrist and psychologist. The interview guide consisted of open-ended questions probing participants' perceptions of factors that either facilitated or interfered with achieving successful transplant outcomes. Topics included participants' functioning before transplantation, selection and preparation for surgery, and experiences with rehabilitation and regaining function after transplantation.

Interviews were recorded and transcribed verbatim. Thematic analysis of the transcript data from all interviews was performed through development of a coding scheme (collection of codes or words and phrases) and thematic scheme (list of themes, subthemes and hypotheses or short statements). Interview excerpts relevant to each theme were collated using qualitative data analysis software and a thematic map was created to portray the themes and their visual interrelationships.

*Thematic map and results from focus group interviews with upper extremity VCA recipients and their primary caregivers:*

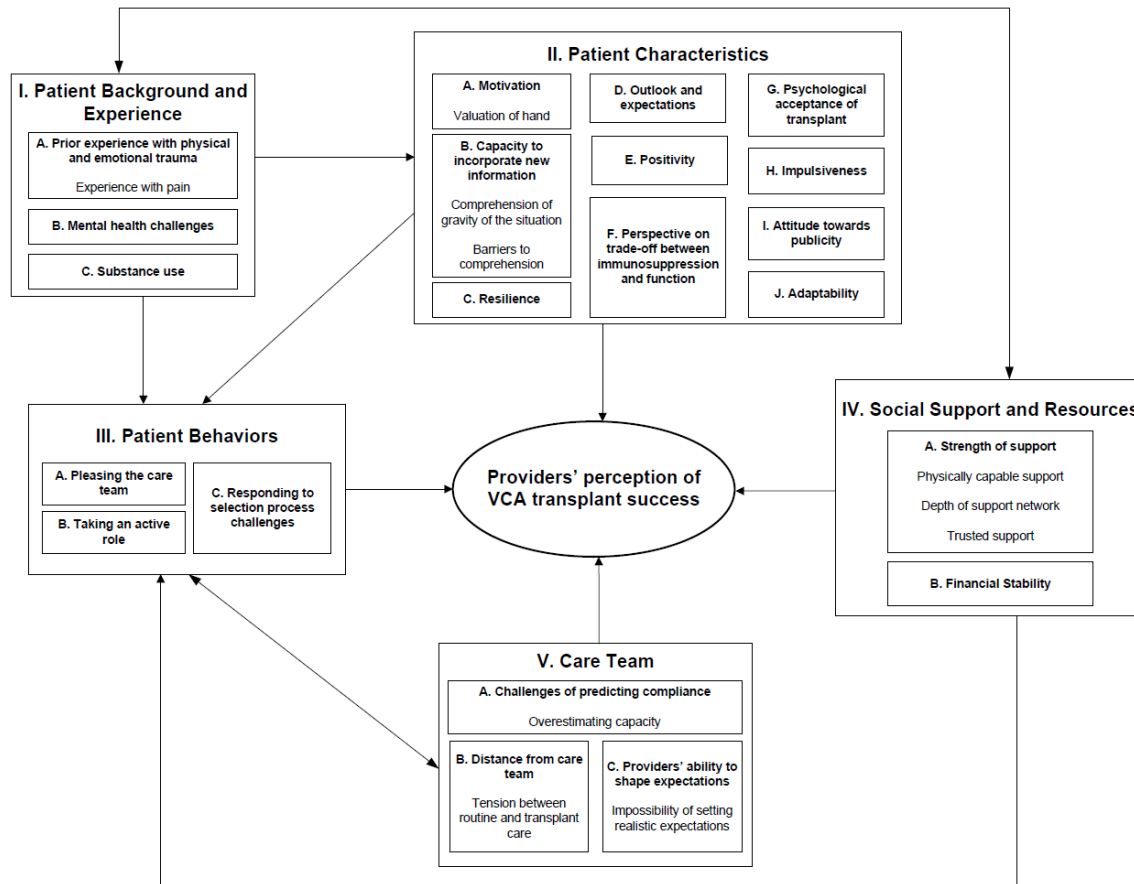


A total of 4 themes encompassing 16 subthemes was identified. Factors that emerged as important to perceived success included realistic expectations of life after transplant, strong social support, and coping strategies including positive framings of one's situation.

The social and expressive use of hands was a powerful motivator for recipients to attempt transplantation. Accurate expectations set forth by the transplant team were found to be limited by the variability of post-transplant function. It was concluded that potential recipients must be comfortable with this uncertainty and accept an unavoidable loss of function before reaching anticipated gains. Recipients expressed a belief that understanding comes only through experience. Given the small number of upper-limb transplants performed to date, opportunities to share experiences and help set expectations are lacking. Recipients at our institution. The fantasy of regaining limbs was found to be a potential barrier to accepting the limitations and a drawback of receiving a transplant. The caregiver has a vital role in supporting the transplant recipient both physically and emotionally, with recipients reporting the recovery to be alienating. Caregivers were described as being vital to the long-term well-being and survival of the transplant. By understanding the impact of one's transplant on the surrounding social support, the recipient can protect these relationships and empathize with recipients' experience. Viewing transplantation as an opportunity for personal growth allowed recipients to focus on positive aspects of the experience, and some made conscious decisions to adopt positive, grateful outlooks. Recipients' spirits were bolstered by small gains in independence and success in completing new tasks, particularly self-care tasks. This tempered the uncertainty of the overall functional outcome.

This qualitative study of transplant recipients and their primary caregiver suggests that transplant success is most likely in recipients demonstrating resilient, creative, positive attitudes with access to strong social support and a deep understanding of expectations.

*Thematic map and results from focus group interviews with experts in the field of VCA:*



A total of 5 themes encompassing 22 subthemes was identified. Factors that emerged as important to perceived success from the provider perspective, included: (1) recipient’s prior experience is believed to determine their ability to cope and adapt after transplantation, (2) behaviors and characteristics influence candidacy and can be predictive of successful outcomes, and (3) social support is essential for improved function and compliance.

Recipients with characteristics of motivation, resilience, adaptability, positive perspective and outlook, and a limited degree of impulsiveness were thought to have greater success after transplantation. Providers recognized their own bias in evaluating candidates with combinations of these unique characteristics, coining it as the “X factor”, feeling that these candidates will adapt to the rigorous selection process and be better prepared for challenges after transplantation.

These characteristics were also felt to be demonstrated by recipients who take an active role in their care. It was felt that providers should maintain a level of caution and skepticism because candidates may attempt to unintentionally attempt to please the care team to improve their candidacy.

This qualitative study of experts within the field of VCA suggest that motivated recipients with developed coping and resilience; a positive attitude; and stable, physically-able caregivers will have greater success post-transplant.

This concluded aim 2 and all major goals were met. Two manuscripts describing this qualitative work were published in 2021, both in Journal of Hand Surgery (J Hand Surg Am. 2021 Aug;46(8):711.e1-711.e35. doi: 10.1016/j.jhsa.2021.01.001. Epub 2021 Mar 13.) (J Hand Surg Am. 2021 Jul 12;S0363-5023(21)00280-X. doi: 10.1016/j.jhsa.2021.05.005.)

For the third aim, we used the data from aims 1 and 2 to select factors for further study: depression/anxiety, patient's expectations for post-transplantation function, family support, participation in occupational therapy (OT) and punctuality. Factor selection was limited to the five most important variables to allow for meaningful statistical analysis.

We created 32 VCA recipient profile vignettes based on permutation of the five selected psychosocial risk factors. Experts were asked to evaluate a surgical candidate presented in the vignette on a scale of zero to ten, with zero designating poor transplant candidacy, five designating fair-good transplant candidacy, and ten for excellent candidacy. We assembled 100 survey packets which were distributed at the American Society for Reconstructive Transplant (ASRT) Conference in November of 2018 which had 140 registered attendees from 27 transplantation centers across 19 countries. We had a total of 100 survey respondents including surgeons, non-surgeon physicians, non-physician clinicians, and non-clinicians. Each of the 100 packets contained 10 candidate vignettes, yielding a total of 1000 candidate vignettes in the study samples. After excluding vignettes with missing outcome scores, we included 991 vignettes in our analytical sample.

Each packet contained 10 vignettes of hypothetical candidates: one "perfect" candidate vignette with zero risk factors, one "poor" candidate vignette with five risk factors, one vignette with one or four risk factors, and three vignettes with two or three risk factors. We assigned a sampling weight to optimize power for detecting differences in outcomes among candidate vignettes with two or three risk factors.

We assigned a sampling weight to optimize power for detecting differences in outcomes among candidate vignettes with two or three risk factors. Our covariates included: (1) risk score (zero to five) defined as the number of risk factors presented in each vignette, (2) survey participants' age, sex, years in practice, geographic region, and specialty. Each set of vignettes was assembled to ensure that candidate risk factors were equally distributed across samples. We used the Generalized Estimating Equation (GEE) to estimate and compare the surgical candidacy scores across different levels of risk factors, accounting for clustering of vignettes among responders. We developed a summarizing risk score to represent the combined effects of risk factors by weighting every risk factor by corresponding regression coefficient from a multivariable

regression model and their standardized beta coefficient estimates from a more limited second model.

Our initial model (Model 1) contained all covariates. At alpha level of 0.15, we excluded survey respondents' age, specialty, and geographic region from the initial model, and kept depression/anxiety, expectation of post-transplantation function, family support, participation in OT, and punctuality (Model 2). Summarizing Risk score, survey participants' sex, and years of practice were included in the final model (Model 3).

#### Appendix IV. Model Selection

	Model 1	Model 2*	Model 3
Depression/Anxiety	√	√	
Expectation	√	√	
Family Support	√	√	
Participation	√	√	
Punctuality	√	√	
Risk Score (# of risk factors in vignette)	√	√	
Summary Risk Score†			√
Age	√		
Years of Practice	√	√	√
Geographic Region	√		
Specialty	√		
Sex	√	√	√

\*: At alpha=0.15, survey participants' age, geographic region and specialty are excluded.

†: Summary Risk Score = 0.7\*depression/anxiety + 1.7\*expectation + 0.7\* family support + 2\*participation in OT + 1.3\*punctuality in OT, weights assigned based on standard beta coefficient estimates from Model 2.

The Summarizing Risk Score depicted the combined effects of depression/anxiety, patients' expectations for post-transplantation function, family support, participation in OT, and punctuality with weights obtained from the Model 2. Among the five risk factors, participation in occupational therapy (OT) and patients' expectations for post-transplantation function had the most influence on the outcome Surgical Candidacy Score.

## Beta Coefficient Estimates for Psychosocial Factors from Model 2

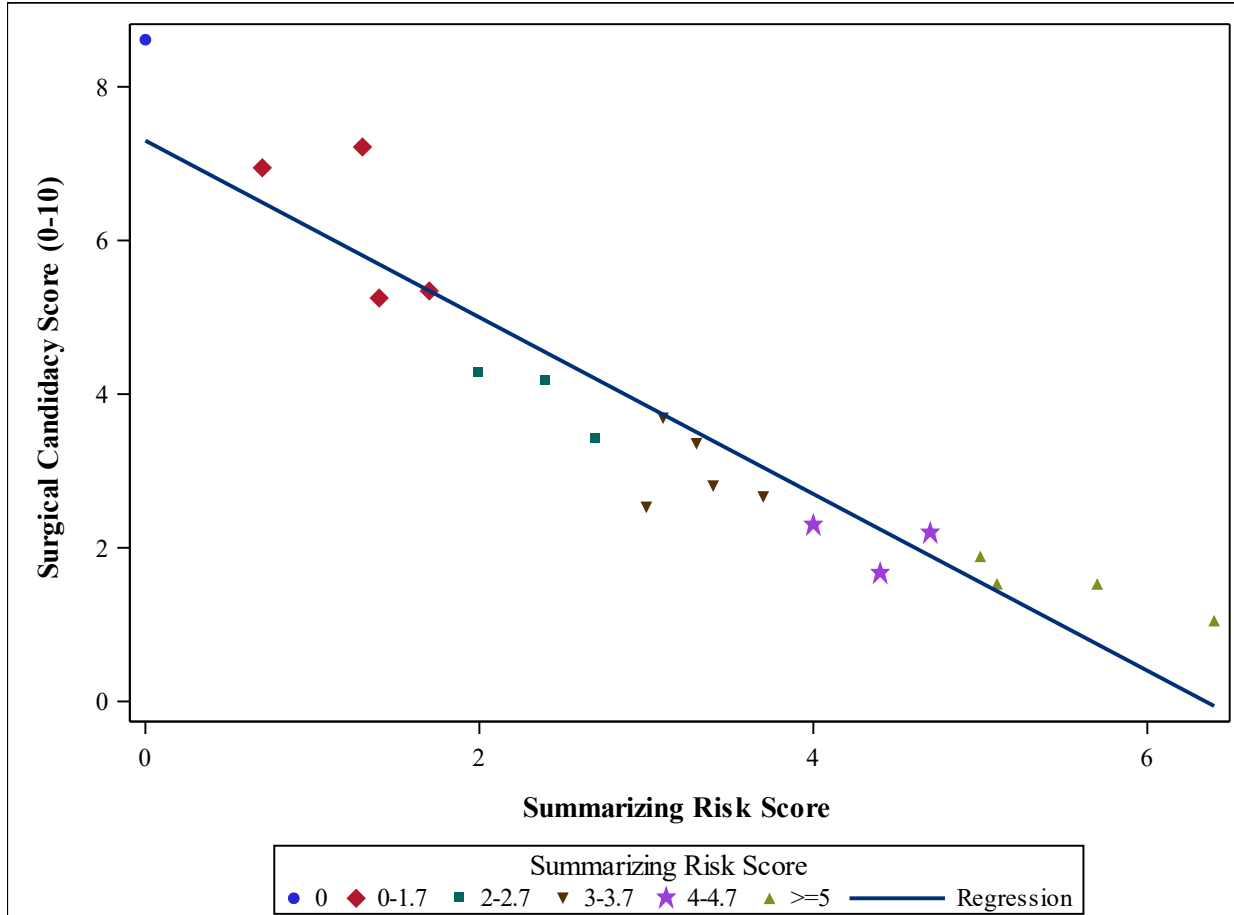
		Estimate	Standard error	Z-value	P-value*
<b>Depression/anxiety</b>	No	0.7385	0.2825	2.61	0.0090
	Yes	0.0000	0.0000		
<b>Expectation</b>	Good/ Realistic	1.7074	0.3009	5.67	<0.0001
	Poor / Unrealistic	0.0000	0.0000		
<b>Family support</b>	Good	0.7072	0.3254	2.17	0.0297
	Poor	0.0000	0.0000		
<b>Participation</b>	Good	2.0171	0.3000	6.72	<0.0001
	Poor	0.0000	0.0000		
<b>Punctuality</b>	Good	1.2653	0.2956	4.28	<0.0001
	Poor	0.0000	0.0000		

\*: Adjusted for number of risk factors in each vignette, survey participants' years of practice, and sex.

†: Summarizing Risk Score (based on standard beta coefficient estimates) =  
 $0.7 * \text{depression/anxiety} + 1.7 * \text{expectation} + 0.7 * \text{family support} + 2 * \text{participation in OT} + 1.3 * \text{punctuality in OT}$ .

Based on standard beta coefficient estimates from Model 2, we created a Summarizing Risk Score by the formula " $0.7 * \text{depression/anxiety} + 1.7 * \text{expectation} + 0.7 * \text{family support} + 2 * \text{participation in OT} + 1.3 * \text{punctuality in OT}$ ". The average surgical candidacy 'fit' score in our candidate vignettes sample was 3.6 (on a scale of zero to ten, ten being the best). Over half of the candidate vignettes in our sample received a Surgical Candidacy Score less than or equal to three (N=569, 57%), and only one hundred-twenty vignettes received a Surgical Candidacy Score greater than seven (N=120, 12%). We observed a general decreasing trend in outcome Surgical Candidacy Score with increasing Summarizing Risk Score.

## Summarizing Risk Score



**Figure.** Least square means of outcome surgical candidacy score regarding summary risk score, adjusted for survey participants' sex and year of practice. The dots are clustered into different risk score groups using different legends (Circle, Diamond, Square, Triangle facing down, Star, and Triangle facing up). The linear regression line indicates that outcome Surgical Candidacy Score decreases rapidly with increasing Summarizing Risk Score.

Our study suggests that negative associations of each psychosocial factor are associated with a perceived expectation of poor UET outcome. Statistical analysis demonstrated participation in OT and patients' expectations of surgical outcomes are the most important of these psychosocial risk factors. Additionally, when negative psychosocial factors are additive when assessing expected outcomes. The opinion of experts demonstrates that a higher presence of risk factors implies worse candidacy with more than five factors being universally predictive of a poor UET outcome. Male health providers and those with 5-10 years of practice tend to be more critical and conservative when assessing the psychosocial impacts identified in our study. In order of importance, poor participation in Occupational Therapy (OT), unrealistic patients' expectations for post-transplantation function, poor punctuality, poor family support, and untreated depression/anxiety were believed to influence outcomes.

Much of our original quantitative data remains incomplete when collating our aim 1 psychosocial survey with IRHCTT data. When applying our Summarizing Risk Score to our original quantitative data, a strong statistical significance was not found. The entirety of this research demonstrates increased negative risk factors correlates to decreased perceived outcomes of success.

This concluded aim 3 and all major goals were met. A manuscript describing this work has been written and submitted for publishing.

Additionally, a subaward contract, local ethics board, and HRPO was approved to perform mirroring focus group interviews with the Medical University of Innsbruck, Austria. Dr. Martin Kumnig has performed focus group interviews on their center's upper extremity transplant recipients, primary caregiver and experts in the field of transplantation. To date, all interviews have been completed and transcribed. Qualitative thematic analysis is currently underway and additional manuscripts are expected in the future.

**Describe the Regulatory Protocol and Activity Status (if applicable).**

Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state "Nothing to Report."

**(a) Human Use Regulatory Protocols**

**TOTAL PROTOCOLS:** State the total number of human use protocols required to complete this project (e.g., 5 human subject research protocols will be required to complete the Statement of Work."). If not applicable, write "No human subjects research will be performed to complete the Statement of Work."

**PROTOCOL(S):** List the identifier and title for all human use protocols needed to complete the project. Include information about the approved target number for clinical significance, type of submission, type of approval with associated dates, and performance status. The following format shall be used:

**Protocol ( of total):**

Protocol [HRPO Assigned Number]:

Title:

Target required for clinical significance:

Target approved for clinical significance:

**Submitted to and Approved by:**

Provide bullet point list of protocol development, submission, amendments, and approvals (include IRB in addition to HRPO).

**Status:**

Report (i) progress on subject recruitment, screening, enrollment, completion, and numbers of each compared to original planned target(s), e.g., number of subjects enrolled versus total number proposed; (ii) amendments submitted to the IRB and USAMRMC HRPO for review; and

(iii) any adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation.

TOTAL PROTOCOLS: 3 – We have broken up our IRB and HRPO by the 3 specific aims

**PROTOCOL (1 of 3 total):**

Protocol [HRPO Assigned Number]: A-20392.1

Title: **Hand Transplant Risk Stratification: Psychosocial Predictors in VCA**

Target required for clinical significance: **Analysis of de-identified data provided by IRHCTT, not involving human subjects.**

Target approved for clinical significance: **Analysis of de-identified data provided by IRHCTT, no involving human subjects.**

**Submitted to and Approved by:**

- IRB, HRPO

**Status:** N/A – not involving human subjects

(i) Number of subjects recruited/original planned target:

Number of subjects screened/original planned target:

Number of patients enrolled/original planned target:

Number of patients completed/original planned target:

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review: N/A

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation: N/A

**PROTOCOL (2 of 3 total):**

Protocol [HRPO Assigned Number]: A-20392.2

Title: **Psychosocial Predictors in VCA**

Target required for clinical significance: **30 subjects**

Target approved for clinical significance: **HRPO agrees this is no greater than minimal risk for enrollment of 30 subjects.**

**Submitted to and Approved by:**

- IRB, HRPO

**Status:**

(i) Number of subjects recruited/original planned target: **20 subjects**

Number of subjects screened/original planned target: **20 subjects**

Number of patients enrolled/original planned target: **20 subjects**

Number of patients completed/original planned target: **20 subjects**

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review: **Amendments approved by both IRB and HRPO. Additional HRPO has been approved for UCLA and has been approved on behalf of the Innsbruck site which has received local IRB approval.**

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation: **N/A**

**PROTOCOL (3 of 3 total):**

Protocol [HRPO Assigned Number]: **A-20392.3**

Title: **Psychosocial Predictors in VCA**

Target required for clinical significance: **20-100 subjects**

Target approved for clinical significance: **No greater than minimal risk for enrollment of 20-100 subjects.**

**Submitted to and Approved by:**

- **IRB. HRPO.**

**Status:**

(i) Number of subjects recruited/original planned target: **20-100 subjects**

Number of subjects screened/original planned target: **100 subjects**

Number of patients enrolled/original planned target: **100 subjects**

Number of patients completed/original planned target: **100 subjects**

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review: **N/A**

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation: **None**

**(b) Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training**

*“Cadaver” is defined as a deceased person or portion thereof, and is synonymous with the terms “human cadaver” and “post-mortem human subject” or “PMHS.” The term includes organs, tissues, eyes, bones, arteries or other specimens obtained from an individual upon or after death. The term “cadaver” does not include portions of an individual person, such as organs, tissue or blood, that were removed while the individual was alive (for example, if a living person donated tissue for use in future research protocols, that tissue is not considered a “cadaver” under this policy, regardless of whether the donor is living or deceased at the time of tissue use).*

**TOTAL ACTIVITIES:** *State the total number of RDT&E, education or training activities that will involve cadavers. If not applicable, write “No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW).”*

**ACTIVITIES:** Provide the following information in a bulleted list for all RDT&E, education or training activities involving human cadavers conducted or supported during the quarter:

- Title of the RDT&E, education or training activity
- SOW task/aim associated with the activity
- Date the activity was conducted
- Identification of the organization's responsible individual (e.g., PI or individual primarily responsible for the activity's conduct)
- Brief description of the use(s) of cadavers in the activity and the total number of cadavers used during the reporting period
- Brief description of the Department of Army organization's involvement in the activity
- Status of document submission and approvals
- Problems encountered in the procurement, inventory, use, storage, transfer, transportation and disposition of cadavers used for RDT&E, education or training. Examples of problems include but are not limited to: loss of confidentiality of cadaveric donors, breach of security, significant deviation from the approved protocol, failure to comply with state laws and/or institutional policies and public relations issues.

**TOTAL ACTIVITIES:**

**ACTIVITIES:**

**(c) Animal Use Regulatory Protocols**

**TOTAL PROTOCOL(S):**

State the total number of animal use protocols required to complete this project (e.g., 2 animal use research protocols will be required to complete the Statement of Work.). If not applicable, write "No animal use research will be performed to complete the Statement of Work."

**PROTOCOL(S):**

List the identifier and title for all animal use protocols needed to complete the project. Include information about the approved target number for statistical significance, type of submission, type of approval with associated dates, and performance status.

The following format shall be used:

**Protocol ( of total):**

Protocol [ACURO Assigned Number]:

Title:

Target required for statistical significance:

*Target approved for statistical significance:*

**Submitted to and Approved by:**

*Provide bullet point list of protocol development, submission, amendments, and approvals (include IACUC in addition to ACURO).*

**Status:**

*Provide bullet point list of performance and/or progress status relating to the above protocol and discuss any administrative, technical, or logistical issues that may impact performance or progress of the study (e.g. animal use protocol needs revision to minimize animal suffering, animal protocol modification to include additional staff) for the above ACURO approved protocol.*

TOTAL PROTOCOL(S):

**PROTOCOL ( of total):**

Protocol [ACURO Assigned Number]:

Title:

Target required for statistical significance:

Target approved for statistical significance:

**Submitted to and Approved by:**

**Status:**

**What opportunities for training and professional development has the project provided?**

Nothing to report.

**How were the results disseminated to communities of interest?**

Publication in the medical literature including open access articles. Three papers have been published, a fourth is being submitted and a fifth paper comparing the Austrian data will be written and submitted following completion of thematic analysis of the Austrian data.

**What do you plan to do during the next reporting period to accomplish the goals?**

We continue to complete the thematic analysis for the Austrian work and will complete a final paper. All other work, including patient and provider interviews, has been completed.

**4. IMPACT:**

The selection of transplant candidacy is currently an inherently subjective process. This research sought to determine psychosocial factors associated with perceived success in upper extremity VCA in attempt to improve assessment of candidacy.

With the first aim of this study, quantitative analysis of international data combined with psychosocial surveys demonstrated anxiety, depression, PTSD, participation in occupational therapy, expectations for post transplant function, and social support were associated with post-surgical transplant status (intact versus removed). Among this, anxiety, PTSD and post-transplant expectations reached statistical significance.

With the second aim, qualitative focus group interviews of transplant recipient and the primary caregivers suggested that transplant success is most likely in recipients demonstrating resilient, creative, positive attitudes with access to strong social support and a deep understanding of expectations. Similarly, qualitative focus group interviews of experts in the field of VCA suggests that motivated recipients with developed coping and resilience; a positive attitude; and stable, physically-able caregivers will have greater success post transplant.

Finally, in aim 3, our quantitative vignette survey suggests that negative associations of each psychosocial factor are associated with a perceived expectation of poor transplantation outcome. In order of importance, poor participation in Occupational Therapy (OT), unrealistic patients' expectations for post-transplantation function, poor punctuality, poor family support, and untreated depression/anxiety were believed to influence outcomes.

Ultimately, this extensive body of work demonstrates that negative psychosocial factors lead to worse transplantation outcomes and an optimal candidate demonstrates qualities of resiliency, positive attitude, well developed coping, deep understanding of expectations who have access to physically-able caregivers. Our Summarizing Risk Score  $0.7*depression/anxiety + 1.7*expectation + 0.7*family\ support +$

$2*participation\ in\ OT + 1.3*punctuality\ in\ OT$  can be references to determine candidacy from a psychosocial perspective. While there are many factors needed to determine appropriate candidacy, this can be an additional consideration during assessment.

We believe that awareness of all of these psychosocial risk factors will help to raise awareness of the need to consider psychosocial concerns in this unique patient population and to help providers focus on addressing these areas to optimize candidates prior to transplantation.

**What was the impact on other disciplines?**

We expect the findings be applicable broadly to major upper extremity injury patients in general.

**What was the impact on technology transfer?**

Nothing to report.

**What was the impact on society beyond science and technology?**

Nothing to report.

**5. CHANGES/PROBLEMS:**

**Changes in approach and reasons for change**

Nothing to report.

**Actual or anticipated problems or delays and actions or plans to resolve them**

Minor delays in manuscript preparation and publication due to the COVID-19 pandemic and shut down of our non-essential staff and slowdowns in publications.

**Changes that had a significant impact on expenditures**

Nothing to report.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

Nothing to report.

**Significant changes in use or care of vertebrate animals.**

Nothing to report.

**Significant changes in use of biohazards and/or select agents**

Nothing to report.

**6. PRODUCTS:**

• **Publications, conference papers, and presentations**

**Journal publications.**

Kinsley, Sarah E.; Song, Shuang; Petruzzo, Palmina; Sardu, Claudia; Losina, Elena; Talbot, Simon G. Psychosocial Predictors of Upper Extremity Transplantation Outcomes: A Review of the International Registry 1998–2016. *Plastic and Reconstructive Surgery - Global Open*. 8(9):e3133, September 2020.

Kinsey, SE, Lenhard NK, Lape EC, Shah SB, Edwards RR, Katz JN, Talbot SGT. Perceived Success in Upper-Extremity Vascularized Composite Allotransplantation: A Qualitative Study. *J Hand Surg AM*. 2021 Aug;46(8):711.31-711.e35.

Kinsley SE, Williams EE, Lenhard NK, Shah SB, Edwards RR, Katz Jn, Talbot SG. A Provider Perspective of Psychosocial Predictors of Upper-Extremity Vascularized Composite Allotransplantation Success. *J Hand Surg AM*. 2021 Jul 12:S0363-5023(21)00280-X.

Pending: Kinsley SE, Song S, Losina E, Talbot SG. Psychosocial risk stratification of upper extremity vascularized composite allotransplantation candidates.

**Books or other non-periodical, one-time publications.**

Nothing to report.

**Other publications, conference papers, and presentations.**

Two post presentations at the Military Health System Research Symposium, Orlando, FL, August, 2019

- Qualitative evaluation of psychosocial predictors of outcomes in upper extremity vascularized composite allotransplantation
- Psychosocial predictors of outcomes in upper extremity vascularized composite allotransplantation with mock patient vignettes

• **Website(s) or other Internet site(s)**

Nothing to report.

• **Technologies or techniques**

Nothing to report.

• **Inventions, patent applications, and/or licenses**

Nothing to report.

• **Other Products**

Nothing to report.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### What individuals have worked on the project?

Name: Simon Talbot  
Project Role: Principal Investigator  
Researcher Identifier (e.g. ORCID ID):  
Nearest person month worked: 4  
Contribution to Project: Directs and oversees all phases of the study.

Name: Robert Edwards, PhD  
Project Role: Co-Investigator  
Researcher Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.96 - Unchanged  
Contribution to Project: Directs qualitative portion of study and assists in all phases of study.

Name: Jeffrey Katz, MD, MSc  
Project Role: Co-Investigator  
Researcher Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.96 - Unchanged  
Contribution to Project: Assists in all phases of the study, particularly qualitative research and case vignette development.

Name: Elena Losina, PhD  
Project Role: Co-Investigator  
Researcher Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.96 - Unchanged  
Contribution to Project: Assists in all aspects of study and ensures methodologic and statistical needs are met. Involved in statistical analysis, development and testing of vignettes and will oversee finalizing of all data collection forms.

Name: Sejal Shah, MD  
Project Role: Co-Investigator  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.96 - Unchanged  
Contribution to Project: Assist in all phases of study and development of focus group interviews and analysis of data.

Name: Matthew Carty, MD  
Project Role: Co-Investigator  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.48 - Unchanged  
Contribution to Project: Assists in study planning and focus group expert interviews.

Name: George Dyer, MD  
Project Role: Co- Investigator  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.48 - Unchanged  
Contribution to Project: Assists in study planning and focus group expert interviews.

Name: Sarah Kinsley  
Project Role: Research Study Coordinator  
Research Identifier:  
Nearest person month worked: 1.28  
Contribution to Project: Assists with data collection, basic analysis and to ensure that each phase of the project remains on schedule.

Name: Nora Lenhard  
Project Role: Research Assistant  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 2.4 - Unchanged  
Contribution to Project: Responsible for performing literature reviews and development of study materials.

Name: Emma Williams  
Project Role: Research Assistant  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 2.4 - Unchanged  
Contribution to Project: Responsible for performing qualitative literature reviews and analysis.

Name: Christine Gude  
Project Role: Administrator  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 1.2 - Unchanged  
Contribution to Project: Coordination of travel arrangements and conference meetings.

Name: Faith Selzer, PhD OrACORe  
Project Role: Project Manager  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 0.96 - Unchanged  
Contribution to Project: Oversees secondary data analysis and data collection projects.

Name: Shuan (Zoey) Song  
Project Role: Data Analyst  
Research Identifier (e.g. ORCID ID):  
Nearest person month worked: 6 - Unchanged  
Contribution to Project: Statistical analysis, development and implantation of data for vignettes.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to report.

**What other organizations were involved as partners?**

Organization Name: Medical University of Innsbruck, Austria  
Location of Organization: Innsbruck, Austria  
Partner's contributing to the project: Dr. Martin Kumnig PhD  
Financial Support: Subaward of USAMRAA Grant Funds Approved April 1, 2019  
In-Kind Support: N/A  
Facilities: N/A  
Collaboration: N/A  
Personnel exchanges: N/A

Organization Name: University of California, Los Angeles, CA  
Location of Organization: Los Angeles, CA  
Partner's contributing to the project: Elisa Moreno  
Financial Support: N/A  
In-Kind Support: N/A  
Facilities: N/A  
Collaboration: N/A  
Personnel exchanges: N/A

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**



# Psychosocial Predictors in VCA

Log Number: RT160066

Award Number: W81XWH-17-1-0400

PI: Simon Talbot, MD

Org: Brigham and Women's Hospital

Award Amount: \$1M

**Study/Product Aim(s)**

- Hand transplantation has moved from an experimental option for a few amputees to, at some institutions, the standard of care. This transition has occurred without a comprehensive analysis of the factors that contribute to the success or failure of these unique transplants. We believe that demographics, anatomic factors, medical comorbidities, social situations, psychiatric/psychological factors, therapy involvement, and logistical factors have a complex interplay to contribute to a good outcome. The objective of this study is to better delineate psychosocial factors associated with outcomes in this group of upper extremity transplant patients.

**Approach**

- Specific Aim 1: To evaluate prospectively collected data on the International Registry of Hand and Composite Tissue Transplantation to determine variables associated with transplant "success"
- Specific Aim 2: To elucidate core factors involved in transplant success and failure utilizing qualitative research methods.
- Specific Aim 3: To develop a model, based on expert opinion, to help objectify the evaluations of hand transplant patients.

Perceived Success in Upper-Extremity Vascularized Composite Allotransplantation: A Qualitative Study  
 Jeffrey N. Katz, MD, PhD  
 International Registry 1998-2016

Psychosocial Predictors of Upper Extremity Transplantation Outcomes: A Review of the International Registry 1998-2016  
 Sarah E. Lerner, MD, PhD  
 International Registry 1998-2016

A Provider Perspective of Psychosocial Predictors of Upper-Extremity Vascularized Composite Allotransplantation Success  
 Sarah E. Lerner, MD, PhD, James R. Connor, MD, PhD, Robert E. Edwards, MD, PhD  
 International Registry 1998-2016

Abstracts from the above studies are included in the main body of the report.

Published works in Journal of Hand Surgery and Plastic Reconstructive Surgery Global Open

**Timeline and Cost**

Activities	2017	2018	2019	2020
Evaluate prospectively collected data				
Qualitative assessment of core factors in transplant success and failure				
Develop model to objectify evaluations of transplant candidates				
Estimated Budget (\$K)	337	335	321	

Updated: 10/22/2021

**Goals/Milestones**

- CY17-18 Goal** – Evaluate data collected from IRHCTT to determine factors of transplant success
  - IRB and HRPO Approval
  - Obtain and analyze IRHCTT data
- CY18-19 Goal** – Qualitative assessment of core factor
  - Focus group interviews
  - Analyze qualitative data from interviews
- CY19-20 Goal** – Develop model to objective evaluation of hand transplant candidacy
  - Develop survey for clinical experts
  - Obtain survey results and analyze data from clinical experts
  - Begin manuscript journal submission
  - Determine statistical model and score to correlate with existing patients

Comments/Challenges/Issues/Concerns: None

Budget Expenditure to Date:

Actual Expenditure: \$992,281.26 (indirect costs \$554,370.71)

## **9. APPENDICES:**

Perceived Success in Upper-Extremity Vascularized Composite Allotransplantation: A Qualitative Study

A Provider Perspective of Psychosocial Predictors of Upper-Extremity Vascularized Composite Allotransplantation Success

Psychosocial Predictors of Upper Extremity Transplantation Outcomes: A Review of the International Registry 1998-2016