Technology Assessment Program

Office of Patient Care Services

A SYSTEMATIC REVIEW OF CLINICAL PREDICTORS OF OUTCOMES IN ADULTS WITH RECENT MAJOR LOWER LIMB AMPUTATION

Author: Elizabeth Adams, RRT, MPH
Research Analyst

Contributors: Karen Flynn, MS, DDS
Program Manager

Elaine Alligood, MLS
Information Specialist

Report Released: February 2005

A SUMMARY FOR HTA REPORTS
Copyright INAHTA Secretariat 2001

VATAP is a member of the International Network of Agencies for Health Technology Assessment (INAHTA) [www.inahta.org]. INAHTA developed this checklist© as a quality assurance guide to foster consistency and transparency in the health technology assessment (HTA) process. VATAP will add this checklist© to its reports produced since 2002.

This summary form is intended as an aid for those who want to record the extent to which a HTA report meets the 17 questions presented in the checklist. It is NOT intended as a scorecard to rate the standard of HTA reports – reports may be valid and useful without meeting all of the criteria that have been listed.

A SYSTEMATIC REVIEW
OF CLINICAL PREDICTORS OF OUTCOMES
IN ADULTS WITH RECENT MAJOR LOWER LIMB AMPUTATION
(February 2005)

Item	Yes	Partly	No
Preliminary			
1. Appropriate contact details for further information?	√		
2. Authors identified?	√		
3. Statement regarding conflict of interest?			√
4. Statement on whether report was externally reviewed?	√		
5. Short summary in non-technical language?	√		
Why?			
6. Reference to the question that is addressed and context of the assessment?	√		
7. Scope of the assessment specified?	√		
8. Description of the health technology?	√		
How?			
9. Details on sources of information?	√		
10. Information on selection of material for assessment?	√		
11. Information on basis for interpretation of selected data?	√		
What?			
12. Results of assessment clearly presented?	√		
13. Interpretation of the assessment results included?	√		
What Then?			
14. Findings of the assessment discussed?	√		
15. Medico-legal implications considered?			√
16. Conclusions from assessment clearly stated?	√		
17. Suggestions for further actions?	√		

ACKNOWLEDGMENTS

The VATAP gratefully acknowledges the contributions of the following reviewers. Participation as a reviewer does not imply endorsement.

Valerie A. Lawrence, MD
Physician Advisor, VA Technology Assessment Program
Audie L. Murphy VA Medical Center
Associate Professor, Department of Medicine
University of Texas Health Science Center at San Antonio
San Antonio, Texas

Dr. Víctor Sarmiento González-Nieto
Specialist in Rehabilitation Medicine
Andalusian Health Service
Spain

Dr. Anita Beelen
Department of Rehabilitation
Academic Medical Centre
Amsterdam
The Netherlands

TABLE OF CONTENTS

EXECUTIVE SUMMARY

- The VA Physical Medicine and Rehabilitation (PM&R) Program Office asked the VA Technology Assessment Program (VATAP) to review the scientific evidence of clinical predictors of outcomes in adult patients with recent major lower limb amputation. The information would be used to update VA's Lower Extremity Amputee Algorithm Guide, an evidence-based protocol of rehabilitative care for the lower extremity amputee used for quality improvement. Identifying the most powerful predictors of outcome could help clinicians direct health care resources toward individuals who are most likely to benefit from specific rehabilitation interventions of care.

- VATAP conducted a qualitative systematic review of the literature published from 1990 through February 2004 in multiple electronic databases. Using published evidence-based resources for evaluating studies of clinical predictors, VATAP applied a framework to appraise study quality and a hierarchy of evidence to appraise the stage of development of clinical predictors that supports their use in clinical practice. To synthesize data from comparable study populations, VATAP organized studies by recruitment setting and cause of amputation.

- The best available evidence consists of seven preliminary studies evaluating predictors of short-term and intermediate outcome measures associated with prosthetic use and mobility, primarily in older patients with nontraumatic causes of amputation. The results are highly dependent on the patient sample, the screening methods used to select a subset of potential predictor variables, the definition of those predictor variables and the outcome measures used.

- Advancing age is a negative predictor for most outcome measures identified in this review, but not by itself. Results along with clinical experience suggest that baseline pre-amputation functional capability, general health status, and socioeconomic situation may also be important predictors of prosthetic use and functional ability, but most of these predictors were defined differently across studies or identified only in single studies.

- These studies represent the weakest evidence associated with quantifying the individual contributions of various predictive factors to outcome measures. Predictors derived from these studies would need to be validated in the veteran population, or a comparable population, before incorporating them into clinical practice. In addition, a set of potentially important predictors of resource utilization relevant to VA, patient-focused measures of prosthetic use, functional outcome and patient satisfaction, and long-term outcome measures such as health-related quality of life needs to be explored.

- This systematic review identified promising predictors for further study as well as deficiencies in the published evidence that should be remedied with rigorous research. With its sizeable amputee population and expertise in rehabilitation and clinical research, VA is poised to advance the body of evidence from derivation studies to validation studies and impact analyses needed for improving the quality of rehabilitation care for amputees within an evidence-based and patient-focused framework.

A SYSTEMATIC REVIEW OF CLINICAL PREDICTORS OF OUTCOMES IN ADULTS WITH RECENT MAJOR LOWER LIMB AMPUTATION

PURPOSE

The VA Physical Medicine and Rehabilitation (PM&R) Program Office asked the VA Technology Assessment Program (VATAP) for a literature review to update VA's Lower Extremity Amputee Algorithm Guide (NCCC 1996). The Guide is an evidence-based protocol of rehabilitative care for the lower extremity amputee and has been used as an effective tool for quality improvement. It emphasizes a patient-centered, interdisciplinary care model across a continuum of rehabilitation care. PM&R specifically asked VATAP to review the scientific evidence of clinical predictors of outcomes in adult patients with recent major lower limb amputation published since 1990.

BACKGROUND

Amputation can signify a visible sign of sacrifice made in military service or the complex health care needs of an aging veteran population. Amputation constitutes a major health challenge to VA and to the population it serves, underscored by the heavy burden of health system use among veteran amputees; veteran amputees also have poor postoperative and late survival outcomes after major lower extremity amputation (Feinglass 2001; Cruz 2003).

In 1993 VA established the Preservation-Amputation Care and Treatment (PACT) Program, which represents a model of clinical care designed to prevent or delay amputation through coordinated, proactive early identification of patients who are at risk of limb loss, primarily veterans with diabetes (VHA 2001). The PACT Program also *"provides the medical and prosthetic resources required to reduce the risk of amputations and to enable the patient to function at his/her maximum level of independence"* (VA Rehabilitation 2004). The Prosthetic and Sensory Aids Service (PSAS) Strategic Healthcare Group furnishes prosthetics and assistive devices to VA amputees.

Amputation risk profiles from FY99 discharge data indicate that a significant portion of veteran amputees has a history of open wound or infection, severe systemic disease, and functional limitations resulting in a partially or totally dependent functional status; amputation rates were highest among Native American veterans and Black veterans and lowest among White veterans and Asian American veterans (HAIG 2001). FY99-FY03 VHA discharge data confirm that amputation rates increase with age and are higher among diabetics (Hawley 2004).

Since the PACT Program was implemented, the total number of lower extremity amputations per year has decreased from approximately 9,000 in 1993 (VHA 2001) to

less than 5,100 in FY03 (Hawley 2004). In recent years, VA has begun to experience an increase in the number of new, younger veterans with traumatic amputation as a result of military action in Afghanistan and Iraq. Careful selection of patients and rehabilitative intervention is essential for allowing amputees to achieve their maximal level of functional independence.

To that end, identifying factors from methodologically sound research that can predict patient outcomes might assist the clinician in meeting many objectives along the rehabilitation continuum of care. For example, predictors identified prior to rehabilitation and during the rehabilitation process could help direct interventions that will improve amputees' adjustment, reintegration and health-related quality of life. Among older and sicker amputees, predictors documented prior to rehabilitation could pinpoint who might be more amenable to cosmetic or functional prostheses and who might achieve higher levels of functional performance, thus avoiding harm to the patient and wasting precious resources. Predictors documented during the rehabilitation process could help identify who among younger and healthier amputees might do best with more expensive and complex prostheses, and could identify the abilities required to improve prosthetic function among all prosthetic users.

METHODS

For this report, VATAP appraised the evidence published since 1990 of clinical prediction rules used to identify variables that predict outcomes in adult lower limb amputees. Clinical prediction rules (CPRs) are clinical decision-making tools that use systematic data collection and multivariable regression analyses to quantify the individual contributions of potential predictor variables in order to indicate the probability of disease or outcome or to suggest a diagnostic or therapeutic course of action (Laupacis 1997). Potential predictor variables include patient demographics, symptoms, risk factors at presentation, history characteristics, and comorbidity.

McGinn (2000) points out the advantages of CPRs to clinical decision-making:

> *"Clinical experience provides us with an intuitive sense of which findings on history, physical examination, and investigation are critical in making an accurate diagnosis, or an accurate assessment of our patients' fate. While often extraordinarily accurate, this intuition may sometimes be misleading. Clinical prediction rules [CPR] attempt to formally test, simplify, and increase the accuracy of clinicians' diagnostic and prognostic assessments…CPRs are most likely to be useful in situations where decision making is complex, where the clinical stakes are high, or where there are opportunities to achieve cost savings without compromising patient care."*

McGinn further describes the development of a CPR in three phases:

1. Derivation—identifying predictive factors of clinical outcomes in discrete study populations (creating the rule);
2. Validation—confirming the results of derivation studies in different study populations and settings (testing the rule);
3. Impact analysis—assessing the impact of the rule on clinical behavior, and ultimately patient care.

Most of the literature on CPRs consists of derivation studies, without subsequent validation studies. CPRs that have been derived but not validated should not be considered ready for clinical application.

The methodologic quality of both derivation and validation studies should be assessed to evaluate the strength of the results and if further validation studies are warranted. However, even the most accurate CPRs may not be implemented into daily practice, affect clinical behavior, or improve patient care. Impact analysis allows evaluation of the usefulness of a CPR, its ease of use, and other potential barriers to implementation into daily practice.

VATAP used a systematic review method to appraise the scientific evidence of CPRs for outcomes in adult lower limb amputees. A systematic review requires an *explicit research question* to guide the framework for the review and *transparent design* to prevent bias and improve the accuracy of findings, while emphasizing *quality* of the available evidence. National-level policy makers and providers in many countries have adopted research evidence as the basis for policy decisions, so a valid reflection of the scientific evidence is important.

While there has not been a set of quality criteria established for systematically reviewing studies of CPRs, Altman (2001) suggests the importance of several key methodological aspects related to study validity. These principles are derived from clinical epidemiology and biostatistics as well as common sense. VATAP used published evidence-based methods to conduct a qualitative systematic review of CPRs.

Search strategy

VATAP searched the literature published from 1990-February 2004 in MEDLINE®, EMBASE®, Current Contents® and Science Citation Index® on Dialog® using multiple text words and indexing terms for lower limb/extremity amputation concepts and combined them with terms for rehabilitation, prognosis, recovery of function, quality of life, activities of daily living, treatment outcome, analytic methods. Additionally, VATAP searched the Cochrane Library (March 2004, Issue 1) of evidence-based reviews and protocols along with manual searching of end reference lists. These searches yielded a total of 581 citations. A review of titles and abstracts indicated 128 potentially relevant citations.

Inclusion criteria

The following criteria were applied to the citations for inclusion in the review:

- Target population was adult patients with lower extremity amputation;
- A method of multivariable analysis was used to derive predictive factors (studies reporting data only from univariate analyses were excluded);
- Randomized trial or cohort study designs were used to determine predictor variables;
- Adequate number of outcome events or subjects was present based on the "Rule of five" (Peduzzi 1996) (applying the "Rule of five" means that a study must have at least five outcome events per predictor entered into the model or at least five subjects per variable entered into the regression equation, depending on the type of analysis, to ensure the stability and validity of the model);
- Statistical importance of predictors was expressed by using a standardized regression coefficient, p-value, or amount of explained variation;
- Studies had clearly described methods for collecting data with validated methods (studies attempting to validate data collection instruments were excluded);
- Systematic literature reviews of relevant CPRs had sufficiently stated methods to assess validity and reproducibility;
- Full text articles were published in English or with a structured English language abstract (no meeting abstracts or editorials);
- If the same investigator group published more than one study for the same purpose with the same population, only the largest or most recent version was included (to eliminate redundant information).

Quality appraisal

VATAP adopted methodologic standards from a variety of published sources to develop a quality appraisal framework for studies of clinical predictors (Table 1) (McGinn 2000; Randolph 1998; Laupacis 1997; Peduzzi 1996).

Table 1. Framework for evaluating studies of clinical prediction rules

Study attributes	Standards
Internal validity	
Study objective(s)	• Primary goal of original study described—was the original objective to develop a clinical prediction rule or to do something else?
Study perspective	• Prospective or retrospective data collection clearly stated
Representative study sample	• Target population to which the results are to be applied sufficiently described • Consecutive or random sample of study subjects used • Important patient characteristics described • Study setting described
Follow up	• Completeness in either the derivation set or the validation set described • Sufficient length of time stated (usually a minimum of one year post amputation, depending on the outcome measured)
Potential predictors	• Clear, clinically sensible and reproducible definition of potential predictors presented • Measurement of predictors fully described • Process for identifying potential predictors described • Assessment of predictor variable blinded to outcome measure—

Study attributes	Standards
	either prospective data collection used or blinding clearly stated in retrospective study
Outcome measures	• Clear and objective definitions presented • Primary outcome measure or surrogate measure should be clinically important • Outcome measurement blinded to prognostic information
Analysis	• Multivariable analysis described and used to evaluate independence of each potential predictor • Magnitude of risk associated with each predictor quantified • Able to calculate events per predictor variable or determine number of subjects present in the study to apply rule of five
Results	
Performance of clinical prediction rule	• Ability to discriminate between patients with higher risk of encountering the outcome from those with lower risks presented • Amount of uncertainty or variability associated with the results described
External validity	
Reproducibility	• Predictive power maintained in a different sample of patients prospectively
Applicability to clinical care	• Similarity of study population to clinical population described • Results presented in a clinically meaningful way • Easy to use
Impact on clinical care	• Improvement in clinical accuracy and clinically important magnitude of change in accuracy described • Changes in clinical decision making linked to improvements in care

Adapted from McGinn 2000; Randolph 1998; Laupacis 1997; Peduzzi 1996.

VATAP then employed a hierarchy of evidence from McGinn (2000) to appraise the stage of development of a CPR that supports the use of a CPR intended for clinical practice.

Table 2. Hierarchy of evidence for clinical prediction rules

Level	Evidence	Comment
I	Rules that can be used in a wide variety of settings with confidence that they can change clinician behavior and improve patient outcomes	At least one prospective validation in a different population and one impact analysis, demonstrating change in clinician behavior with beneficial consequences.
II	Rules that can be used in various settings with confidence in their accuracy	Demonstrated accuracy in either one large prospective study including a broad spectrum of patients and clinicians, or validated in several smaller settings that differ from one another.
III	Rules that clinicians may consider using with caution and only if patients in the study are similar to those in the clinical setting	These rules have been validated in only one narrow prospective sample.
IV	Rules that need further evaluation before they can be applied clinically	These CPRs have been derived but not validated or have only been validated in split samples, large retrospective databases, or by statistical techniques. • In order to graduate from Level IV, subsequent studies must involve the actual use of the rule by investigators in their study population.

*Adapted from McGinn (2000)

RESULTS

Of the 128 articles initially retrieved for possible inclusion, 108 studies were excluded. Reasons for exclusion were: randomized trial or cohort study designs not used; studies of only univariate analyses, adolescent populations, or upper limb amputees; inadequate ratio of events per predictor variable in the multivariable analysis or insufficient sample size; insufficient reporting of methods, or; insufficient reporting of results (eg. failure to report statistics that would enable the reader to discern statistical significance or predictive power of results). Thirteen articles provided background information for the report.

The best available evidence of clinical predictors of outcomes is seven Level IV derivation studies of cohorts of adults with lower limb amputation. Six of the cohort studies were prospective, and one (Dawson 1995) was an historical (retrospective) cohort. Three (Hermodsson 1998; Bosse 2002; Schoppen 2003) were multi-site studies. To allow for meaningful synthesis of comparable study populations, VATAP organized studies by recruitment setting and cause of amputation. Rehabilitation care planning and outcomes are associated with different amputation types, but because few studies evaluated discreet amputee populations, organizing studies by amputation type was not attempted. Table 3 provides an overview of the included studies with the corresponding data abstraction tables. Table 4 summarizes study findings. Details of included studies are abstracted in Tables A through C in the Appendix.

Table 3. Overview of studies that met inclusion criteria for review

Note: all studies were cohort studies.

Non-traumatic = ≥ 70% total study subjects with non-trauma-related etiology
Traumatic = ≥ 70% total study subjects with trauma-related etiology

Hospital inpatient = subjects recruited as hospital inpatients pre- or post-amputation in acute care setting
Rehab Unit = subjects recruited in either a hospital inpatient rehab unit or specialized rehab center
Community = subjects recruited post rehab discharge, usually in residential dwelling

	Recruitment Setting Population (# studies)			
Causes	**Hospital inpatient**	**Rehab Unit (referral-based)**	**Community**	TOTAL
Non-traumatic	**3 Table A**	**3 Table B**		**6**
Traumatic	**1 Table C**			**1**
TOTAL	**4**	**3**	**0**	**7**

The majority of studies were conducted with male patients age 60 years or older with primarily non-traumatic (vascular) causes of unilateral transtibial amputation (Tables A and B). The research objectives of these studies were to identify factors predictive of improved rehabilitation and functional outcomes associated with prosthetics use and mobility. Hermodsson (1998) also identified survival rate and prosthetic function among amputees eight years post amputation and explored whether background factors of female transtibial amputees with good function differed from those of males with good

function. Traballesi (1998) also assessed factors predictive of extended nursing home stays one-year post amputation and of lowering the length of stay in a rehabilitation unit. Comorbidities such as diabetes, cardiovascular disease, and cerebrovascular disease were frequently present in these populations, reflecting chronic systemic diseases common to an aging population.

All studies included consecutive series of patients or defined cohorts of patients who were completely followed from enrollment through analysis, except for Pohjolainen (1991) in which 14 patients were excluded from analysis without explanation. Studies excluded subjects with severe cognitive impairment, severe disability without walking ability pre-amputation, and stump problems. Cohorts were either hospital inpatients or referral-based amputees, meaning groups of patients either referred for rehabilitation or those who had already undergone a rehabilitation program. The referral-based studies represented highly selected populations of amputees who would be most amenable to rehabilitation with assistive devices and would likely demonstrate improved outcomes of care. Hermodsson (1998) and Jones (2001) considered transtibial amputees only, and Traballesi 1998 included transfemoral amputees only. All other studies included a mix of amputation types, and only one (Bosse 2002) identified amputation level as a potential predictor on correlational analysis, although it was not found to be an independent predictor after multivariable analysis.

Treatment intervention, generally defined as “rehabilitation”, “prosthetic fitting”, or “prosthetic training”, was variable reflecting the individualized treatment planning in rehabilitation. Traballesi (1998) standardized treatment for study subjects specifically over three hours per day for six days per week, and Bosse (2002) defined treatment as either reconstruction or amputation.

Length of follow up varied depending on the study objective, recruitment population and outcomes measured. Follow up among hospital inpatients ranged from two weeks post amputation (Schoppen 2003) to several years post amputation (Bosse 2002; Dawson 1995; Hermodsson 1998). Follow up among referral subjects ranged from four weeks after admission to rehabilitation (Jones 2001) or until discharge from the rehabilitation unit (Traballesi 1998) or one-year post amputation (Pohjolainen 1991).

Potential predictors were generally screened from a defined list of patient characteristics that were statistically significant on correlational analysis, except for Pohjolainen (1991) who identified ten potential predictors for multivariable analysis. The comprehensiveness of the initial screening list of patient characteristics varied across studies, as did the definition of some common variables such as comorbidity.

Studies generally considered short-term and intermediate outcome measures to define degree of independence in activities of daily living, prosthetics use and mobility. Studies described outcome measures clearly and objectively, but not consistently. For example, the timed-up-and-go test, walking distance, walking time, Rivermead Mobility Index and outdoor walking ability were used to define mobility at different lengths of follow up. Only Bosse (2002) and Schoppen (2003) considered long-term outcome

measures using the Sickness Impact Profile to evaluate quality of life as a measure of health status or dysfunction generated by amputation at two years post amputation and one year post amputation, respectively.

Use of blinded assessment of predictor variables and outcome measures was notably absent in the evidence base. Ideally, bias is minimized when outcome measures are assessed without knowledge of the predictor variables, and vice versa. The importance of blinding depends on whether the outcome measure or potential predictor is subjective (very important) or objective (less or not important). In a prospective study, potential predictors are assessed prior to, and without knowledge of, the outcome event. Therefore, blinded outcome assessment should be clearly stated. Use of blinded assessment of predictors and outcome measures in retrospective studies should also be clearly stated. All but one prospective study (Bosse 2002) failed to state their use of blinded outcome assessment. The one historical cohort (Dawson 1995) included in this review failed to clearly state its use of blinded assessment of either the independent predictor variables or outcome measures.

Based on the inclusion criteria used in this review, all studies used some type of multivariable analysis to determine the independence of each potential predictor, and all had an adequate number of outcome events or subjects to ensure the stability and validity of their analysis. All conveyed some sense of the statistical importance of the independent predictors, but few conveyed the amount of uncertainty or variability associated with the results.

For hospital inpatients with non-traumatic causes of lower limb amputation (Table 4):

- All three studies reported pre-amputation age < 65 years was an independent predictor of a number of outcome measures--returning home ambulating with an assistive device, receiving a prosthesis, and function outcome at one year post amputation measured with the SIP-68, GARS and the TUG scores.
- In one study (Schoppen 2003), age at amputation, comorbidity, poor one-leg balance on the unaffected limb at two weeks post amputation, and mental performance based on the 15-word test predicted functional outcome using the SIP-68 in 69% of amputees. Age, one-leg balance and the 15-word test predicted functional outcome using the GARS score in 64%, while age and one-leg balance test predicted functional outcome using the TUG test in 42%.
- Good pre-amputation walking ability, pre-amputation independent level of self care, living status, left side amputation and male gender were positive independent predictors of various outcomes in single studies.

For referral-based patients with non-traumatic causes of lower limb amputation (Table 4):

- Three studies reported advancing age, generally defined as > 65 years, was a significant negative predictor for all outcomes related to prosthetics use and mobility; it was not a significant predictor for length of stay (Traballesi 1998) or standard weight bearing at week four of rehabilitation (Jones 2001).

- One study (Traballesi 1998) indicated advancing age, longer interval between amputation and rehabilitation admission, Doppler features on admission and Barthel Index score on admission predicted improvement in mobility at discharge in 23% of transfemoral amputees. Advancing age and presence of diabetes on admission predicted improvement in activities of daily living (change in Barthel Index score) in 14% of transfemoral amputees, while a higher Barthel Index score on admission and male gender predicted length of stay in 16% of transfemoral amputees.
- One study (Jones 2001) found advancing age and standard weight bearing at four weeks post amputation predicted prosthetic use at week four of rehabilitation in 66% of transtibial amputees, while standard weight bearing at the beginning of rehabilitation and perceived pain at week four post amputation predicted standard weight bearing at week four of rehabilitation in 56% of transtibial amputees.
- Other independent positive predictors of outcomes in single studies were employment status, cerebrovascular history, time lag between surgery and prosthetic fitting, previous vascular surgeries, and phantom and stump pain at prosthetic fitting.

For inpatients with traumatic causes of lower limb amputation, one study (Bosse 2002) met the inclusion criteria (Table 4). The study compared functional outcomes of reconstruction versus amputation in younger males (mean age early 30s) with primarily transtibial amputations, who were recruited from trauma centers and followed for at least two years after injury.

- Predictors of poor health status two years post amputation using the Sickness Impact Profile score were: nonwhite race; lack of private health insurance or Medicaid; poor social support network; low self-efficacy; smoking; less than high school education; involvement in disability-compensation litigation, and rehospitalization for a major complication.

CONCLUSIONS

The best evidence of clinical predictors of outcomes in adults with recent lower limb amputation is seven Level IV derivation studies (Table 4). While Level IV studies represent the weakest evidence associated with quantifying the individual contributions of various predictive factors to outcome measures, the results may help VA clinicians and investigators identify the most promising predictors to consider for further study. Clinical prediction rules (CPRs) derived from these studies need to be validated by applying the rule to the veteran population, or a comparable population, before incorporating them into clinical practice.

Studies focused on predictors of primarily short-term and intermediate outcome measures associated with prosthetic use and mobility during or immediately following rehabilitation in older patients with nontraumatic causes of amputation. Advancing age is a negative predictor for most outcome measures identified in this review, but not by itself. Results suggest, along with clinical experience, that baseline pre-amputation functional capability, general health status, and socioeconomic situation may also be important predictors of prosthetic use and functional ability, but most of these predictors

were defined differently across studies or identified only in single studies. In addition to age, a set of potentially important predictors of resource utilization, patient-focused measures of prosthetic use, functional outcome and patient satisfaction, and long-term outcome measures such as health-related quality of life needs to be explored in the veteran population.

Results in this review are highly dependent on the patient sample, the screening methods used to select a subset of potential predictor variables, and the outcome measures used, and they may not be generalizable to the veteran population. Furthermore, differences in processes of care, which were not addressed in the research, may confound the results. In particular:

- Conclusions should take into account the distinct amputee populations of interest based on cause and type of amputation along the continuum of care. Using only amputees selected for rehabilitation as study subjects may overestimate many of the outcomes associated with prosthetic rehabilitation in general amputee populations.
- Screening methods for selecting potential predictor variables used in multivariable analysis generally relied on correlational analysis, but the comprehensiveness of the initial list of potential predictors considered for correlational analysis varied across studies.
- The main outcome measures addressed prosthetics use and mobility of lower extremity amputees, yet the evidence shows a lack of consensus in the choice and definition of these outcomes measures.
- Use of blinded assessment of predictor variables and outcome measures should be clear to the reader, but was notably absent in the evidence base, particularly blinded assessment of outcome measures in prospective studies.

For these reasons and the preliminary nature of the evidence, additional longitudinal studies are needed to derive a comprehensive set of independent predictors suitable for the veteran population. The independent predictors identified in this review and in subsequent research should be validated in prospective research in a VA or comparable population of sufficient sample size before being incorporated into the VA Lower Extremity Amputee Clinical Algorithm Guide.

DISCUSSION

Narrative reviews of the literature found that prognostic factors such as increasing age, poor compliance, phantom limb pain and comorbidity (i.e. cardiac disease, stroke and cognitive problems) were unfavorably associated with outcome in amputees (Pernot 1997; Kent 1999; Geertzen 2001). Successful results in rehabilitation were associated with the patient's general condition, the amputation level, good covering of the stump with muscles, a nontraumatic operation technique, and the absence of stump pain. To assist in planning rehabilitation capacity, the authors recommended prospective research to develop a pre-amputation prosthetic profile including prognostic factors related to the influence of disabilities, their social network and other environmental factors on functional prognosis, as well to define the burden of the amputee on society.

In this VATAP review, amputation level, important for rehabilitation care planning, was not an independent predictor of outcome. In fact, of the studies of patients with different amputation levels, only one screened amputation level as a *potential* predictor (Bosse 2002). Comorbidity may also play a predictive role, particularly in a high-risk veteran population, but the results in this review were inconsistent across studies and depended on the definition of comorbidity and outcome measured. Patients with severe cognitive limitations, severe mobility limitations and stump problems were excluded from studies in this review, and effects of compliance as a predictive factor could not be determined. Presence of phantom limb pain and stump pain was an independent negative predictor of walking ability with prosthesis in one study (Pohjolainen 1991).

Laupacis (1997) summarized why variables do not become part of the CPR: 1) the variable has no predictive value; 2) the variable has predictive value on its own but it does not add predictive value to the rule that is not provided by other variables, or; 3) the assessment of the variable is unreliable to justify inclusion in the rule. Results from cohort studies included in this review suggest the need for further study before accepting or abandoning these variables as potential predictors.

Other narrative reviews commented on the limitations of the evidence with respect to variation in populations studied and outcome measures used (Turner-Stokes 1997; Rommers 2001; Deathe 2002; Jelic 2003). Little is known about long-term outcome measures related to rehabilitation goals, in particular, health-related quality of life in discrete amputee populations such as: 1) the older amputee with vascular causes of amputation who either ambulates with prosthesis or with other assistive devices; 2) the bilateral amputee, or; 3) the traumatic amputee. Outcome measures used in rehabilitation research are not always focused on the individual's rehabilitation goals, leading to a mismatch between the amputee's needs and the researcher's needs (Pernot 1997). Legro (1999) identified four themes of interest from the veteran amputee's perspective about living with a prosthesis that may help identify areas for future patient-focused outcomes research: fit of the socket with the residual limb; aspects of mechanical functioning; aesthetic and functional qualities; and professional or organizational support.

Finally, systematic reviews play an important role in evaluating evidence of clinical predictors, but they are not without challenges. Altman (2001) discussed common problems associated with systematic reviews of prognostic studies such as identifying all relevant studies (since studies of prognosis can take on many forms) and publication bias. There are also limitations in the evidence related to inadequate reporting of methods, variations in methods, inadequate reporting of results, and variation in reporting of results, which make synthesis of results difficult.

Many of these problems were also identified in this review. The overall preliminary nature of the evidence base argues for conducting qualitative systematic reviews in the area of clinical predictors for patients with lower limb amputation, but it argues against

using quantitative approaches such as meta-analysis, the results of which may be distorted by heterogeneous study design or quality.

The main limitations in this review were restricting studies to those published in English and after 1990, which would have omitted studies published in other languages or prior to 1990 that could have informed the analysis. Since some of the other reviews, which considered literature published prior to 1990, commented on similar limitations in the evidence, it is unlikely that well-designed derivation or validation studies existed which would have altered the findings of this review. The search retrieved studies published in all languages, and review of title and abstract information of non-English citations did not uncover any that would have been potentially relevant to the review. Nonetheless, the possibility of omitting relevant studies published in other languages exists.

VATAP identified several cross-sectional studies in the evidence base that were used to determine factors associated with patient outcome. It is not uncommon to confuse these studies with true derivation studies, and may explain some of the differences in results across literature reviews. However, cross-sectional studies are not appropriate for deriving clinical predictors, because they look at associations between variables and outcomes at one point in time and are not designed to predict outcome over time. A reliable predictive study requires a well-defined cohort of patients at the same stage of their disease or treated in the same way (Altman 2001). Therefore, studies of predictive factors, even Level IV derivation studies, require a longitudinal design. This report identified several cohort studies that lay the foundation for an evidence base of clinical prediction rules to be validated for use in clinical practice.

The main advantage of this systematic review is in identifying deficiencies in the evidence base using rigorous methodology, which can be used to direct future research toward studies of higher quality. Identifying the most powerful predictors of positive (and negative) outcome could help clinicians identify which amputees will do well (or poorly), and thereby improve outcomes by directing health care resources toward those who are most likely to benefit from rehabilitation interventions of care. To that end, VA is poised, by virtue of its sizeable amputee population and its expertise in rehabilitation and clinical research, to advance the body of evidence from derivation studies to validation studies and impact analyses. These studies are needed to improve the quality of rehabilitation care within an evidence-based and patient-focused framework.

Table 4. Summary of multivariable studies of clinical prediction rules for patients with lower limb amputation

Note: Abbreviations are at the end of the table.

Definitions:

Non-traumatic = ≥ 70% total study subjects with non-trauma-related etiology
Traumatic = ≥ 70% total study subjects with trauma-related etiology
Mixed = study includes subjects with different causes of amputation, not meeting the 70% threshold above

Hospital inpatient = subjects recruited as hospital inpatients pre- or post-amputation in acute care setting
Rehab Unit = subjects recruited in either a hospital inpatient rehab unit or specialized rehab center
Community = subjects recruited post rehab discharge, usually in residential dwelling

Study	Study size (N)/ Perspective	Outcome measure	Results: after multivariable analyses (Statistically significant results p<0.05 reported)		Level of Evidence
			Significant predictors	Predictors not significant	
From Table A. Hospital inpatients with non-traumatic causes of LLA					
Dawson 1995	81 R	Returning home either ambulating with a prosthesis or in a wheelchair	• Living alone pre-amputation (RR 0.3, 95% CI 0.1-0.5, p<0.001) • Advanced age > 65 yrs pre-amputation (RR 0.5, 95% CI 0.3-0.9, p<0.05)	• Functional level of self care pre-amputation	**IV**
Dawson 1995	81 R	Mortality	• Dependent pre-amputation level of self-care (RR 1.9, 95% CI 1.1-3.5, p<0.05)	• Living alone pre-amputation • Advanced age > 65 yrs pre-amputation	**IV**
Dawson 1995	81 R	Walking ability post amputation	• Dependent pre-amputation level of self-care (RR 0.2, 95% CI 0.08-0.5, p<0.05)	• Living alone pre-amputation • Advanced age > 65 yrs pre-amputation	**IV**
Hermodsson 1998	71 P	Receiving a prosthesis	• Decreasing age (p=0.015) • Left side amputation (p=0.0004) • Good pre-amputation walking ability (either walking alone or outdoors) (p=0.007) • Not using a wheelchair pre-amputation (p=0.020)	• Concomitant diseases	**IV**
Hermodsson 1998	49 P	Prosthetics use 6 months post-amputation	• Being male (p=0.006) **(+)** • Good pre-amputation walking ability (walking alone outdoors) (p=0.013)	• Dummy variables used in analyses not defined	**IV**
Schoppen 2003	37 P	Functional outcome (SIP-68) at one year post amputation	• Age at amputation (β=.25) • Other comorbidity (not cardiopulmonary or diabetes, but other diseases or disabilities not detailed in report) (β=.43) • Poor 1-leg balance on the unaffected limb 2 wks post amputation (β= - .33) • 15-word test (β= -.26) Total R^2 = .69		**IV**
Schoppen 2003	37 P	Functional outcome (GARS) at one year post amputation	• Age at amputation (β= .42) • 1-leg balance (β= - .40) • 15-word test (β= -.32) Total R^2 = .64	• Other comorbidity (not cardiopulmonary or diabetes, but other diseases or disabilities not detailed in report)	**IV**
Schoppen 2003	37 P	Functional outcome (TUG test) at one year	• Age at amputation (β=.19)	• Other comorbidity (not cardiopulmonary or diabetes, but other diseases or disabilities not	**IV**

Study	Study size (N)/ Perspective	Outcome measure	Results: after multivariable analyses (Statistically significant results p<0.05 reported)		Level of Evidence
			Significant predictors	Predictors not significant	
		post amputation	• 1-leg balance (β= - .58) Total R^2 = .42	detailed in report) • Mental characteristics based on 15-word tests	
From Table B. Rehabilitation Unit inpatients with non-traumatic causes of LLA					
Pohjolainen 1991	125 P	Prosthetics use	• Advancing age (*P*<0.05) • In employment (r= 0.18; *P* <0.05) • Cerebrovascular accidents (r = -0.18; *P* <0.05) • Time lag between surgery and prosthesis (r = -0.26; *P* <0.01)	• Gender • Body mass index (kg/m^2) • Previous vascular operations • Smoking • Phantom pain • Time between amputation and first fitting • Employment status pre-amputation	**IV**
Pohjolainen 1991	125 P	Walking distance	• Advancing age (*P*<0.0001) • In employment prior to amputation (r = 0.29; *P* <0.001) • Previous vascular operations (r = -0.17; *P* <0.05) • Phantom and stump pain at prosthetic fitting (r = -0.17; *P* < 0.05)	• Gender • Body mass index (kg/m^2) • Heart disease • Cerebrovascular accidents • Smoking • Time between amputation and first fitting	**IV**
Pohjolainen 1991	125 P	Walking time	• Advancing age (*P*<0.001) • In employment prior to amputation (r = 0.24; *P* <0.05) • Previous vascular operations (r = -0.20; *P* <0.05)	• Gender • Body mass index (kg/m^2) • Heart disease • Cerebrovascular accidents • Smoking • Phantom pain • Time between amputation and first fitting	**IV**
Pohjolainen 1991	125 P	Ability to walk outdoors	• Advancing age (*P*<0.001) • Cerebrovascular accidents (r = -0.17; *P* <0.05) • Phantom and stump pain at prosthetic fitting (r = -0.20; *P* <0.1)	• Gender • Body mass index (kg/m^2) • Heart disease • Previous vascular operations • Smoking • Time between amputation and first fitting • Employment status pre-amputation	**IV**
Traballesi 1998	144 P	Improvement in mobility at discharge (RMI effectiveness)	• Advancing age (β = -0.23; p<0.01) • Longer interval between amputation and rehab admission (β = -0.17; p<0.05) • Doppler features on admission (β = -0.21; p<0.05) • Barthel Index score on admission (β = 0.26; p<0.005) R^2=0.23	• Gender • Amputation side • Comorbidities on admission • Diabetic vs. primary vascular etiology • RMI score on admission	**IV**
Traballesi 1998	144 P	Improvement in ADL at discharge (change in Barthel Index score)	• Advancing age (β = -0.24; p<0.01) • Presence of diabetes on admission (β = 0.23; p<0.05) R^2=0.14	• Gender • Amputation side • Days of interval between amputation and rehab admission • Comorbidities • Doppler features • BI score on admission • RMI score on admission	**IV**

Study	Study size (N)/ Perspective	Outcome measure	Results: after multivariable analyses (Statistically significant results p<0.05 reported)		Level of Evidence
			Significant predictors	**Predictors not significant**	
Traballesi 1998	144 P	Length of stay	• Lower Barthel Index score on admission (β = - 0.24; p<0.01) • Male gender (β = 0.24; p<0.01) R^2=0.16	• Age • Amputation side • Days of interval between amputation and rehab admission • Comorbidities • Diabetic vs. primary vascular etiology • Doppler features • RMI score on admission	**IV**
Jones 2001	27 P	Prosthetics use (walking velocity) at week 4 of rehab	• Advancing age (β = -0.75) • Standard weight bearing (SWB) at wk 4 post amputation (β = 0.42) R^2=0.66; p<0.001 Pain played a role in walking velocity through a relationship mediated by its direct effect on SWB. SWB is a predictor of walking velocity that might be altered through pain reduction, wound-healing and rehab interventions	• SWB at entry • Pain level at entry • Pain at week 4 post amputation	**IV**
Jones 2001	27 P	SWB at week 4 of rehab	• SWB at entry (β = 0.46) • Perceived pain at wk 4 post amputation (β = -0.48) R^2=0.56; p<0.001	• Age • Pain level at entry	**IV**
From Table C. Hospital inpatients with traumatic LLA					
Bosse 2002	130 P	Self-reported health status at 2 years using Sickness Impact Profile	• Non-Caucasian race (p<0.01) • No insurance or having Medicaid 4-24 mo post injury (p<0.01) • Poor social support network (p<0.01) • Low level of self-efficacy (p<0.01) • Baseline smoking status (p<0.01) • Involving the legal system for injury compensation (p<0.01) • < High school education vs. some college (p<0.05) • Rehospitalized for a major complication (p<0.05) Comparison of functional outcome at two years between patients undergoing reconstruction vs. amputation found no differences	• Treatment (amputation level) • Income level • High school graduate vs. some college • No health insurance 0-3 mo post injury	**IV**

ADL, activity of daily living
AKA, above the knee amputation
BDI, Beck Depression Inventory
BI, Barthel Index
BKA, below the knee amputation
CST, Cognitive Screening Test
CWT, Stroop Color-Word Test
CVD, cerebrovascular disease
GARS, Groningen Activity Restriction Scale
LE, lower extremity
LLA, lower limb amputation
LOS, length of stay
OMFAQ, OARS Multidimensional Functional Assessment Questionnaire
P, prospective
PVD, peripheral vascular disease
QOL, quality of life
R, retrospective
RMI, Rivermead Mobility Index
SATPRO, questionnaire for measuring amputee's satisfaction (Bilodeau 1999)
SIP-68, Sickness Impact Profile, 68 item version
SSL12-I, Social Support Questionnaire-Interactions, 12 item version
SPMSQ, Short Portable Mental Status Questionnaire (Pfeiffer 1975)
SWB, static weight bearing
TFA, transfemoral amputation
TTA, transtibial amputation
TUG, Timed up and go test

END REFERENCES

Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. *New England Journal of Medicine,* 2002; 347: 1924-1931.

Cruz CP, Eidt JF, Capps C, Kirtley L, Moursi MM. Major lower extremity amputations at a Veterans Affairs hospital. *American Journal of Surgery,* 2003; 186: 449-454.

Dawson I, Keller BP, Brand R, Pesch-Batenburg J, Hajo van Bockel J. Late outcomes of limb loss after failed infrainguinal bypass. *Journal of Vascular Surgery,* 1995; 21: 613-622.

Deathe B, Miller William C, Speechley M. The status of outcome measurement in amputee rehabilitation in Canada. *Archives of Physical Medicine and Rehabilitation,* 2002; 83: 912-918.

Feinglass J, Pearce WH, Martin GJ, Gibbs J, Cowper D, Sorensen M, et al. Postoperative and late survival outcomes after major amputation : findings from the Department of Veterans Affairs National Surgical Quality Improvement Program. *Surgery,* 2001; 130: 21-29.

Geertzen JHB, Martina JD, Rietman HS. Lower limb amputation Part 2: Rehabilitation - A 10 year literature review. *Prosthetics and Orthotics International,* 2001; 25: 14-20.

HAIG. Healthcare Analysis and Information Group. VHA Office of Policy and Planning. US Dept Veterans Affairs. Accessed: September 22, 2004. Part II: LEA Rates, Comorbid conditions, and Outpatient Utilization. [web site]. http://vaww.va.gov/haig/AMP/AMP8999II.pdf.

Hawley G. *Personal Communication with:* Adams E. VHA Patient Treatment File. *Format*: Personal Communication; October 4, 2004.

Hermodsson Y, Ekdahl C, Persson BM. Outcome after trans-tibial amputation for vascular disease. A follow-up after eight years. *Scandinavian Journal of Caring Sciences,* 1998; 12: 73-80.

Jelic M, Eldar R. Rehabilitation Following Major Traumatic Amputation of Lower Limbs - A Review. *Critical Reviews in Physical and Rehabilitation Medicine,* 2003; 15: 235-252.

Jones ME, Bashford GM, Bliokas VV. Weight-bearing, pain and walking velocity during primary transtibial amputee rehabilitation. *Clinical Rehabilitation,* 2001; 15: 172-176.

Kent R, Fyfe N. Effectiveness of rehabilitation following amputation. *Clinical Rehabilitation,* 1999; 13: 43-50.

Laupacis A, Sekar N, Stiell IG. Clinical prediction rules. A review and suggested modifications of methodological standards. *JAMA,* 1997; 277: 488-494.

Legro MW, Reiber G, del Aguila M, Ajax MJ, Boone DA, Larsen JA, et al. Issues of importance reported by persons with lower limb amputations and prostheses. *Journal of Rehabilitation Research and Development,* 1999; 36: 155-163.

McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS. Users' guides to the medical literature: XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. *JAMA,* 2000; 284: 79-84.

NCCC. National Center for Cost Containment. US Dept Veterans Affairs. Accessed: September 22, 2004. Stroke/Lower Extremity Amputee Algorithims Guide. [web site]. http://vaww.va.gov/haig/algorithms/algorithms.pdf.

Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol,* 1996; 49: 1373-1379.

Pernot HF, de Witte LP, Lindeman E, Cluitmans J. Daily functioning of the lower extremity amputee: an overview of the literature. *Clinical Rehabilitation,* 1997; 11: 93-106.

Pohjolainen T, Alaranta H. Predictive factors of functional ability after lower-limb amputation. *Annales Chirurgiae et Gynaecologiae,* 1991; 80: 36-39.

Randolph AG, Guyatt GH, Calvin JE, Doig G, Richardson WS. Understanding articles describing clinical prediction tools. Evidence Based Medicine in Critical Care Group. *Critical Care Medicine,* 1998; 26: 1603-1612.

Rommers GM, Vos LD, Groothoff JW, Eisma WH. Mobility of people with lower limb amputations: scales and questionnaires : a review. *Clinical Rehabilitation,* 2001; 15: 92-102.

Schoppen T, Boonstra A, Groothoff JW, de Vries J, Goeken LN, Eisma WH. Physical, mental, and social predictors of functional outcome in unilateral lower - limb amputees. *Archives of Physical Medicine and Rehabilitation,* 2003; 84: 803-811.

Traballesi M, Brunelli S, Pratesi L, Pulcini M, Angioni C, Paolucci S. Prognostic factors in rehabilitation of above knee amputees for vascular diseases. *Disability and Rehabilitation,* 1998; 20: 380-384.

Turner-Stokes L, Turner-Stokes T. The use of standardized outcome measures in rehabilitation centres in the UK. *Clinical Rehabilitation,* 1997; 11: 306-313.

VA Rehabilitation Strategic Health Care Group. VA Physical Medicine and Rehabilitation Service. Accessed: September 22, 2004. Physical Medicine and Rehabilitation Service Home Page. http://vaww1.va.gov/health/rehab/SpecPrograms.htm.

VHA. Veterans Health Administration. US Dept Veterans Affairs. Accessed: September 22, 2004. Preservation-Amputation Care And Treatment (PACT) Program. VHA Directive 2001-030. [Web Site]. http://vaww1.va.gov/prosthetics/docs/VHADIRECTIVEONPACT2001-030.pdf.

APPENDIX

Table A. Multivariable studies of predictors of outcome among hospital inpatients with non-traumatic causes of amputation

Note: Abbreviations are at the end of Table C.

Study characteristics	Dawson 1995	Hermodsson 1998	Schoppen 2003
Objective (s)	• To determine late consequences of limb loss after failed infrainguinal bypass (life expectancy and social function) • To determine predictors of late outcome of rehabilitation after major LE amputation due to failed infrainguinal bypass	• To identify prognostic factors at the time of LE amputation for prosthetic fitting and prosthetics use with good function at 6 months • To identify differences in background variables between men and women affecting good function • To identify survival rate and prosthetic function among survivors at 8 years post op	• To study the value of physical, mental, and social characteristics in recent elderly amputees as predictors of functional outcome
Design	• Retrospective • Cohort study	• Prospective • Inception cohort study • Consecutive series	• Prospective • Cohort study • Consecutive series • Some analyses compared with reference populations
Setting (where/when subject recruitment takes place)	• Hospital inpatients who underwent infrainguinal bypass for atherosclerotic occlusive disease between 1958-1989 and who underwent amputation from failed bypass • The Netherlands	• 177 inpatients from amputation registry, OR programs, anesthesia medical records in 1987-1988 at two university hospitals and 3 municipal hospitals in Sweden • Inclusion criteria were unilateral, primary TTA	• Hospital inpatient between October 1997- June 2000 • Residents of one of 3 northern provinces in the Netherlands • 51 patients were excluded due to inability to understand instructions, severe disability without walking ability before amputation for reasons unrelated to PVD, refused to participate, late presentation to the study
Patient characteristics	• N = 81 • BKA 36%, AKA 64%, including 20 revisions; 20% with contralateral limb amputation • Male: 67% • Mean age 68 $\pm$ 12 yrs • HTN 41%, Diabetes 46%, smokers 67%, cardiac history 51%, cerebrovascular history 20% • Cumulative survival rate for patients with vascular amputations: 72% at 1 year; 53% at 3 years; 35% at 5 years	• N = 112; N = 75 alive at 6 months; N = 9 alive at 8 yrs • 100% primary unilateral TTA • Male: 51% • Mean age male 74.1 years (SD = 11.3, range 44-94 yrs); 47% amputees were $\geq$ 80 yrs • 67% with no comorbidities, 39% with diabetes • 52% nonsmokers; 44% married • Pre-op characteristics: 63% lived at home, 58% ambulated alone outdoors, 49% used no walking aids, 13% used wheelchair • Mortality rate: 33% at 6 months post op, 47% at 2 yrs, 92% at 8 yrs	• N=46, follow up data available for 37 • Unilateral BKA or higher (AKA 11%, BKA 72%, KD 17%) • Male: 70% • Age > 60 yrs (mean age 73.9 $\pm$ 7.9 yrs) • Comorbidities: 54% diabetes, 67% cardiopulmonary disease, 80% other (not defined) • 70% lived independently at home 1 year post amputation • 1-yr mortality rate 15%
Treatment Intervention/ Follow up period	• Amputation and rehab varied • Standardized assessment by specialized vascular or rehab unit pre-amputation and annually until death or termination of study in 1991 • Follow up period post amputation ranged 1.5 months to 18 yrs (mean 3.6 yrs)	• Prosthetics fitting-variable intervention • Follow up at 6 months, 8 years post-op	• Rehabilitation variable • Follow up: from 2 weeks to one year post amputation at hospital, rehab center, nursing home and patient residence

Study characteristics	Dawson 1995	Hermodsson 1998	Schoppen 2003
Potential predictors	Statistically significant pre-amputation background characteristics (at p< .05) on correlational analysis: • Age • Residential status (living alone) • Functional level of self care	Statistically significant background characteristics (at p= .05) for prosthetic fit on correlational analysis: • Concomitant diseases (joint, neurological, respiratory, mental diseases, blindness) • Side of amputation • Walking ability pre-amputation • Walking aids pre-amputation • Age Statistically significant background characteristics (at p= .05) for prosthetic function at 6 months on correlational analysis: • Gender • Walking ability pre-amputation	Statistically significant predictors of outcome (at p< .05) measured 2 weeks post amputation on correlational analysis: • Age at amputation • 1-leg standing balance • Comorbidity (diabetes, cardiopulmonary disease, other diseases or disabilities) • Mental characteristics based on BDI, SCT, 15-word, and Stroop CWT tests
Main outcome measures (dependent variable(s))	• Mortality • Social function (probability of returning home post amputation) • Risk of contralateral amputation • Walking ability post amputation with a prosthesis	• Probability of receiving a prosthesis (yes/no) • Probability of good function at 6 months post amputation: • Poor function=variable daily use, unable to walk indoors with assistance, or uses wheelchair most or all of the time • Good function=daily use and able to walk alone or assisted outdoors or alone indoors	Functional outcome measures: • SIP-68 • GARS • TUG Prosthetics use (based on Narang 1984 and Pohjolainen 1990 8-grade scale): • Functional=score 1-IV • Nonfunctional=V-VIII
Results: Significant predictors after multivariable analysis (statistically significant p<.05 results reported)	• Predictor of mortality: self-care dependent (RR 1.9, 95% CI 1.1-3.5, p<0.05) • Predictors of probability of returning home post amputation were living alone pre-amputation (RR 0.3, 95% CI 0.1-0.5, p<0.001) and advanced age > 65 yrs (RR 0.5, 95% CI 0.3-0.9, p<0.05) • Predictor of walking ability post amputation: self-care dependent pre-amputation (RR 0.2, 95% CI 0.08-0.5, p<0.05)	• Predictors of receiving a prosthesis (N = 71) were decreasing age (p=0.015), left side amputation (p=0.0004), and walking ability pre-amputation (either walking alone outdoors (p=0.007) or not using a wheelchair (p=0.020)) • Predictors of good prosthetic function at 6 months post-op was gender (higher among males (p=0.006)) and pre-operative ability to walk alone outdoors (p=0.013)	• Predictors of SIP-68 = Age at amputation (β=.25) + comorbidity other than cardiopulmonary or diabetes (β=.43) + 1-leg balance (β= - .33) + 15-word test (β= -.26) (Total R^2 = .69) • Predictors of GARS = Age at amputation (β= .42) + 1-leg balance (β= - .40) + 15-word test (β= -.32) (Total R^2 = .64) • Predictors of TUG test = Age at amputation (β=.19) + 1-leg balance (β= - .58) (Total R^2 = .42) • No multivariable analysis used for prosthetic use
Authors' comments	• I.e. Age < 65 yrs and living with someone were predictive of successful late outcome as defined by returning home either walking with a prosthesis or in a wheelchair	• Table 3 in article depicts probabilities of prosthetics fitting according to walking characteristics, age and amputation side • Favorable outcomes with left leg amputation merits further study	• Study size limited results and the number of predictors analyzed • Overall patients' functional level was low as indicated by high mean scores on SIP-68 (23.6), GARS (41.2), and TUG test (23.9) • Other variables such as functional ability pre-amputation, motivation, other personal traits not measured due to logistics

Table B. Multivariable studies of predictors of outcome among referral-based rehabilitation unit patients with non-traumatic causes of lower limb amputation

Note: Abbreviations are at the end of Table C.

Study characteristics	Pohjolainen 1991	Traballesi 1998	Jones 2001
Objective	• To identify predictive factors of ambulatory function and prosthetic use after lower limb amputation	To predict rehabilitation potential and identify prognostic factors of patients undergoing AKA for vascular diseases	To study pain during stance and static weight-bearing on the prosthesis as predictors of walking velocity in early prosthetics training in patients with TTA
Design	• Prospective • Cohort study • Consecutive series • Operative data from chart review	• Prospective • Cohort study • Consecutive series	• Prospective • Cohort study • Consecutive series
Setting/ (where/when subject recruitment takes place)	• 155 patients operated on between November 1985 and August 1988 who were referred to the Prosthetic Factory of Helsinki, Finland • Evaluation at prosthetic fitting and follow up at one year post op • 16 died during first post operative year • 14 patients excluded from analysis-no explanation reported	• Consecutive series admitted to IRCCS rehab unit in Rome Italy between 1992-1996 • 129 patients excluded due to BKA, bilateral amputation, previous admission, stump problems or clinical conditions that precluded prosthetic prescription	• Referred to Port Kembla Hospital Rehab Centre from 1995-1997 • 2 patients with stump revision and recurrent stump breakdown were excluded
Patient characteristics	• N = 125 • Male: 71% • BKA 63.5%, AKA 36.5% • Mean age 63 yrs, range 14-87 yrs • Causes of amputation: ischemia due to arteriosclerosis or diabetes 81%, trauma 10%, tumor 6%, other 3% • Accommodation: 88% at own homes, 12% elderly homes • Time between amputation and first prosthesis fitting: ave 16 weeks • At follow up, 5% of BKA and 24% of AKA did not use their prosthesis or only for cosmetic reasons	• N = 144 who completed rehab treatment • AKA 100%, Right side 62.5% • Males: 66% • Mean age 68.7 $\pm$ 10.2 yrs, median 69 yrs) • 100% vascular etiology: 50% diabetes, 50% occlusive vascular pathogenesis • 45% with cardiovascular or respiratory disease, 12% with neurological, 15% other comorbidities • Interval between amputation and rehab admission 107.8 $\pm$ 47.1 days	• N = 27 • TTA 100% • Male: 78% • Mean age 65.4 yrs, range 24-88 yrs • 70% vascular etiology, 15% trauma, 11% infection, 4% neoplasia • Comorbidities not reported • Interval between amputation and rehab admission median 42 days, range 16 to 319 days
Treatment Intervention/ Follow up period	• Prosthetic fitting—variable • Follow up—one year post op	• Standardized treatment 3 hrs per day, 6 days per week • Follow up: rehab admission to discharge median 89 days, range 92.5 $\pm$ 44.7 days	• Prosthetic fitting and training variable • Follow up 4 weeks
Potential predictors	• Age • Gender • Body mass index (kg/m^2) • Heart disease • Cerebrovascular accidents • Previous vascular operations • Smoking • Phantom pain at prosthetic fitting	Admission data: • Age • Sex • Amputation side • Days of interval between amputation and rehab admission • Comorbidities • Diabetic vs. primary vascular etiology	Walking velocity at week 4: • Age • SWB at entry • SWB at week 4 post amputation • Pain level at entry • Pain at week 4 post amputation SWB at week 4:

Study characteristics	Pohjolainen 1991	Traballesi 1998	Jones 2001
	• Time between amputation and first fitting • Employment status pre-amputation	• Doppler features • BI score on admission • RMI score on admission	• Age • SWB at entry • Pain level at entry • Pain at week 4 post amputation
Main outcome measures (dependent variable(s))	• Prosthesis use (hours/day) • Walking distance (in meters) • Walking time (in minutes) • Amount of outdoor walking (minutes/day) • Need for walking aids (seven point scale) • Accommodation situation (4 point scale-living at home alone or with someone, apartment house for the aged, elderly/nursing home, hospital)	• RMI effectiveness • BI effectiveness • LOS • Good autonomy in mobility (RMI score > 11)	• Mean walking velocity, defined as self selected walking velocity at week 4 • SWB at week 4
Results: Significant predictors after multivariable analysis (statistically significant p<.05 results reported)	At $p < .05$, increasing age was a negative predictor of all aspects of physical function; results controlling for age showed: • Predictors of prosthesis use: increasing age ($P<0.05$) in employment ($r= 0.18$; $p<0.05$); cerebrovascular accidents ($r = -0.18$; $p<0.05$); and time lag between surgery and prosthesis ($r = -0.26$; $p<0.01$) • Predictors of walking distance: increasing age ($P<0.0001$); in employment ($r = 0.29$; $p<0.001$); vascular operations ($r = -0.17$; $p<0.05$); and phantom and stump pain ($r = -0.17$;$p<0.05$) • Predictors of walking time: increasing age ($P<0.001$); in employment ($r = 0.24$; $p<0.05$); vascular operations ($r = -0.20$; $p<0.05$) • Predictors of amount of outdoor walking: increasing age ($P<0.001$); cerebrovascular accidents ($r = -0.17$; $p<0.05$) and phantom and stump pain ($r = -0.20$;$p<0.1$) • Need for walking aids: insufficient data to determine adherence to rule of 5 • Accommodation situation: insufficient data to determine adherence to rule of 5	At $p<0.05$ • Predictors of RMI effectiveness: age ($\beta = -0.23$; $p<0.01$), days of interval ($\beta = -0.17$; $p<0.05$), Doppler features ($\beta = -0.21$; $p<0.05$), BI score on admission ($\beta = 0.26$; $p<0.005$); ($R^2=0.23$) • Predictors of BI effectiveness: age ($\beta = -0.24$; $p<0.01$) and diabetic etiology ($\beta = 0.23$; $p<0.05$); ($R^2=0.14$) • Predictors of LOS: BI score on admission ($\beta = 0.24$; $p<0.01$) and male gender ($\beta = -0.24$; $p<0.01$); ($R^2=0.16$) • Predictors of good autonomy in mobility: Insufficient information to determine adherence to rule of 5.	At $p< 0.001$ • Predictors of walking velocity at week 4: age ($\beta = -0.75$) and SWB at week 4 ($\beta = 0.42$); ($R^2=0.66$; $p<0.001$) • Predictors of SWB at week 4: SWB at entry ($\beta = 0.46$) and perceived pain at week 4 ($\beta = -0.48$); ($R^2=0.56$; $p<0.001$)
Authors' comments	• Results suggest more emphasis on early prosthetic fitting is needed, and prosthetics use can be improved by proper prosthetic fitting immediately after active post op training • Prognosis for ambulatory function and prosthetics use is best in younger subjects and working age groups	• Age is the most powerful predictor influencing rehab effectiveness expressed as both mobility and ADL; age is not a contraindication to rehab, but it may reduce the effectiveness of rehab • Good mobility may also have been related to absence of vascular impairment of the residual limb and timely admission to the rehab unit	• SWB is a predictor of walking velocity that might be altered through pain reduction, wound-healing and rehab interventions • Further research is needed to identify other variables that account for the remaining 34% of the variance in walking velocity

Table C. Multivariable study of predictors of outcome among hospital-based subjects with traumatic causes of lower limb amputation

Note: Abbreviations at the end of the table.

Study characteristics	Bosse 2002
Objective	• To compare the functional outcomes of patients from eight level 1 trauma centers who underwent reconstruction vs. amputation
Design	• Prospective • Multicenter • Cohort study • Two orthopedic trauma surgeons who were blinded to patient information and treatment rechecked injury characteristics to adjust for potential confounders. 7.5% of injuries were reclassified based on second evaluation.
Setting/ (where/when subject recruitment takes place)	• Eight level 1 trauma centers in US • 601hospital patients admitted for treatment of high energy trauma below the distal femur between March 1994 and June 1997 • 56 patients excluded because of impaired consciousness, spinal cord deficit, prior amputation, third-degree burns, transferred > 24 hrs after surgery, non-English or non-Spanish speaking, documented psychiatric illness, on active military duty or insufficient follow up at 24 months
Patient characteristics	• N = 130 with amputation, 330 with reconstruction at 24 months • AKA 21%, BKA 61%, KD 11.5%, partial foot 0.7% Reported data based on N=161 amputees at baseline: • Male: 81% • Mean age 35.2yrs; 27% ≥ 40 yrs • 76% Caucasian • Injury severity score: 65.8% <13, 11.8% 13-17, 22% > 17 • Multiple patient characteristics and injury characteristics presented
Treatment Intervention/ Follow up period	• Reconstruction or amputation, not randomized but adjusted for in analysis • Follow up at baseline before discharge, and at 3,6,12, and 24 months after injury
Potential predictors	All patient characteristics associated with an outcome at p<0.10 on correlational analysis: • Treatment (amputation level) • Major complication • Education level • Income level • Race • Health insurance status • Baseline smoking status • Self-efficacy • Social support • Lawyer hired
Main Outcome measures (dependent variable (s))	Self-reported health status measured by SIP
Results: Significant	At p<0.01, factors associated with poor outcome (high SIP score) were: • Non-Caucasian race

Study characteristics	Bosse 2002
predictors after multivariable analysis (statistically significant p<.05 results reported)	• No insurance or having Medicaid • Poor social support network • Low level of self-efficacy • Smoking • Involving the legal system for injury compensation At p<0.05 • < High school education • Rehospitalized for a major complication At p<0.1 • Household income below federal poverty level
Authors' comments	• Patients lost to follow up or with incomplete data were of lower socioeconomic status than those with complete follow up; results may underestimate overall extent of disability • After adjusting for patient and injury characteristics, there were no differences in functional outcomes between patients who underwent reconstruction vs. amputation at two years • Results suggest that major improvements in outcome might require greater emphasis on nonclinical interventions, eg. early intervention by psychosocial and vocational rehab specialists • Interventions aimed at improving patients' perceptions of self-efficacy may benefit those who face a challenging recovery • Generalizability of results beyond patients at level 1 trauma centers is uncertain • Costs of treatment and rehab not considered

ADL, activity of daily living
AKA, above the knee amputation
BDI, Beck Depression Inventory
BI, Barthel Index
BKA, below the knee amputation
CST, Cognitive Screening Test
CWT, Stroop Color-Word Test
CVD, cerebrovascular disease
GARS, Groningen Activity Restriction Scale
LE, lower extremity
LLA, lower limb amputation
LOS, length of stay
OMFAQ, OARS Multidimensional Functional Assessment Questionnaire
P, prospective
PVD, peripheral vascular disease
QOL, quality of life
R, retrospective
RMI, Rivermead Mobility Index
SATPRO, questionnaire for measuring amputee's satisfaction (Bilodeau 1999)
SIP-68, Sickness Impact Profile, 68 item version
SSL12-I, Social Support Questionnaire-Interactions, 12 item version
SPMSQ, Short Portable Mental Status Questionnaire (Pfeiffer 1975)
SWB, static weight bearing
TFA, transfemoral amputation
TTA, transtibial amputation
TUG, Timed up and go test