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PRINCIPAL INVESTIGATOR: Goeran Fiedler

CONTRACTING ORGANIZATION: University of Pittsburgh

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14. ABSTRACT
The goal of this project was to investigate the clinical effectiveness of temperature-controlled prosthesis liners over the long-term. To that end, outcome data were collected at two sites over a total period of 12 months, including two 6-month intervention periods with comparable climate conditions (i.e., equal amounts of cold and warm weather). Results suggest that use of temperature-controlled liners did help reduce days of non-prosthesis use by an average of more than two days per year, a 12% improvement. Self-reported ambulation and health outcomes saw increases of 5.5 and 4% respectively. However, the findings are not considered conclusive since the study had unexpected sample size limitations so that these differences did not rise to the level of statistical significance. Both participant recruitment and retention were challenged by unforeseen factors, most notably the Covid-19 pandemic in the last year of the study period. The study protocol as well as preliminary results have been disseminated in various conference abstracts and as journal manuscripts.

15. SUBJECT TERMS
Limb prosthetics; liner suspension; temperature control; phase-change material

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INTRODUCTION:

The purpose of this research was to investigate the clinical effectiveness of temperature-control prosthesis liners. Such liners, which have recently become commercially available, promise to improve the micro-climate around the residual limb in users of limb prostheses. While it has previously been shown that the new liner is indeed associated with a small but measurable decrease in skin temperature, it has not been quantified how this effect influences clinical outcomes. We hypothesized that the lower temperature will result in better prosthesis utilization, both over the short term (as expressed by daily step counts) and the longer term (days with prosthesis use per year). The rationale for these hypotheses was that a reduction in perspiration would be associated with better prosthesis fit (e.g., less slippage) and socket comfort, both improving biomechanical efficiency and user confidence and reduce adverse events (e.g., skin irritation) to allow for an increase in hours of prosthesis use and in distances covered. These hypotheses were investigated in a multi-site double-blind randomized cross-over study design, intended to generate high-quality evidence.

KEYWORDS:

Artificial limbs, liner suspension, temperature control, phase change materials, clinical trial, outcome assessment, mobility, step count

ACCOMPLISHMENTS:

What were the major goals of the project?

Goals for the project were:

(1) Obtain ethics approval for the study protocol

(2) The recruitment and enrollment of 50 eligible subjects (25 per site),

(3) Fitting them with two sets of prosthesis liners (temperature-controlled intervention and conventional control) to be worn for six-month periods each,

(4) Completing the collection of comprehensive outcomes data, to include daily step counts, self-reported prosthesis evaluation, and physical performance in 6-week intervals across the study period

(5) Analyzing, interpreting, and disseminating the collected data.

What was accomplished under these goals?

(1) Pitt IRB approval was obtained on 10/17/2017 and renewed for another year on 09/28/2018, 10/06/2019, and 09/7/2020. The respective HRPO approval was issued 02/01/2018. The approval at the secondary site, by Widener University IRB was obtained on 09/11/2018 and has subsequently been renewed on 03/29/2019.

(2) The methodology for recruitment and screening has been executed as proposed, using the Pitt+Me research registry, outreach through amputee support groups both offline and online, and disseminating information about the study at local P&O businesses and events. An IRB approved screening script was used to determine eligibility at

intake of a potential participant. Recruitment and screening materials were essentially identical between the two sites.

Across the two study sites, a total of 73 potential participants were contacted and/or screened, of whom 42 were enrolled. Another eight were scheduled for enrollment in the spring of 2020 when study activities had to be paused in the wake of the Covid-19 pandemic response. Seventeen participants did not complete the data collection, and data from another four were excluded from analysis because they had reported recurring prosthesis fitting issues that may have affected outcomes (Figure 1, Table 1).

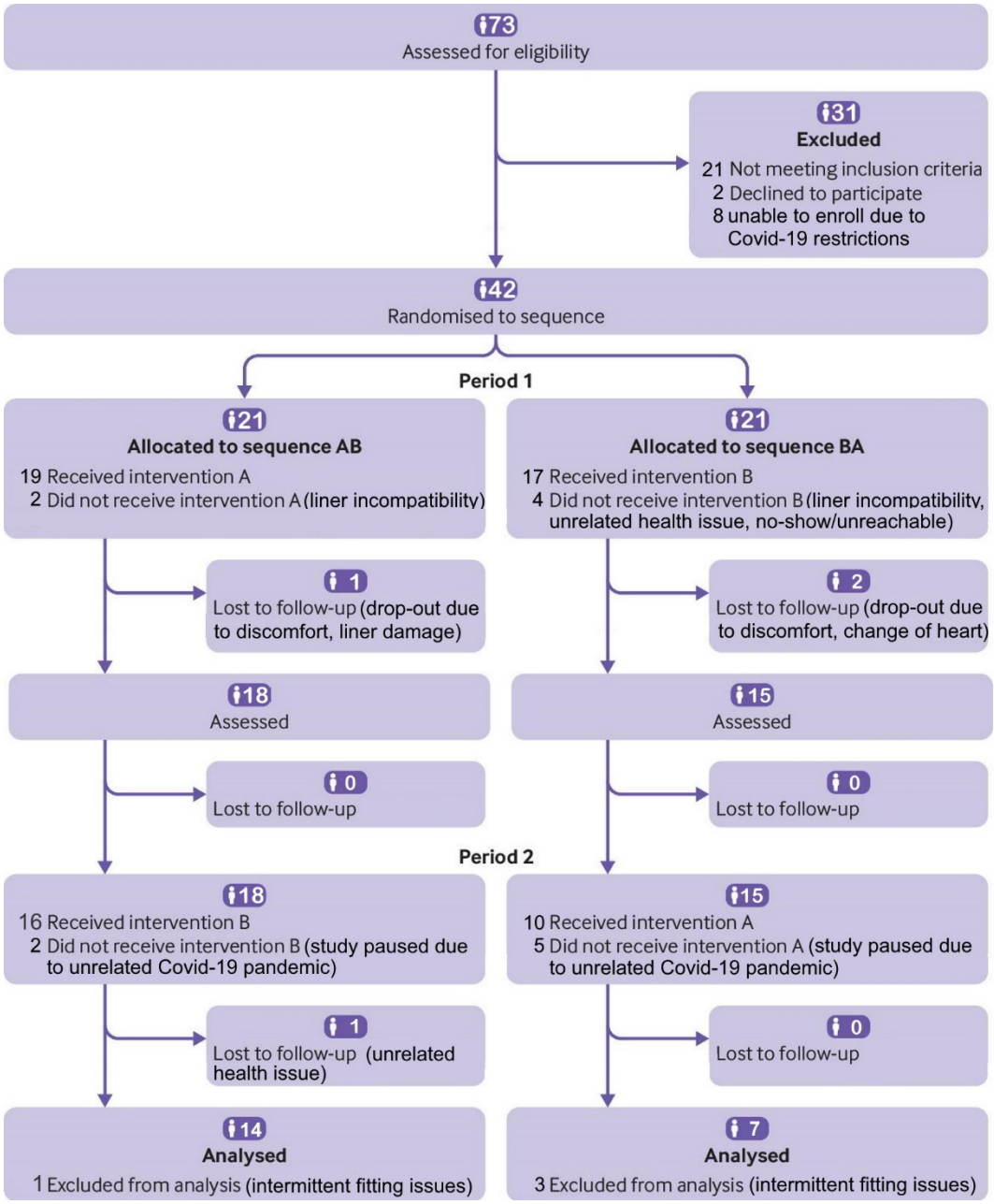

Figure 1: Flow diagram showing recruitment and attrition

Table 1: Study participants by site and cohort. The plans for a third cohort were disrupted by the Covid-19 pandemic and enrollment of these participants was not completed.

Site\cohort	First Cohort (Jan '19 -Jan '20)	Second Cohort (Jul '19 – Jul '20)	Third (planned) Cohort (Apr '20 – Sep '20)	Total sample
University of Pittsburgh	16	13	(4)	29(33)
Widener University	4	9	(4)	13(17)
Total	20	22	(8)	42(50)

(3) Study liners were custom ordered to have identical appearance for purposes of subject and investigator blinding. The liners were provided to the first cohort at the start of the data collection period in January 2019. The second cohort started the protocol in July 2019. This schedule was to assure that an approximately equal number of summer and winter days were part of either 6-month period without having to swap liner types more than once (at the 6-month mark). The planned abbreviated intervention for the 3rd cohort was intended to allow for a comparison of liner types over 2 to 3-month periods around the hot days of summer.

(4) Data collection activities were conducted throughout the study period and entailed follow-up appointments every six weeks, at which points subjects were asked to complete a Prosthesis Evaluation Questionnaire, a PLUS-M mobility questionnaire, and a two-minute-walk test. Step count recordings were read out from a StepWatch monitor that was attached to the subjects' prostheses throughout the study period. In recognizing that shelter-in-place recommendations and other measures in the context of the Covid-19 pandemic were affecting the representativeness of data collected and in order to limit exposure risk to study participants, the in-person follow-up appointments were suspended after February of 2020.

(5) Data analysis methods were adjusted to account for the limitations posed by the unique circumstances. Both descriptive statistics and omnibus significance testing were performed as planned. With found effects not reaching the level of statistical significance, the planned post-hoc analyses became obsolete. Instead, the interpretation of findings was refocused on the effect sizes and potential clinical significance of intervention effects. Additional work has been performed to explore the effects on variables outside of the original scope of the study. Dissemination efforts resulted in two journal manuscripts and three conference presentations (abstracts attached below). These products include an abstract and journal paper about the study protocol, which we believe may be adoptable for future randomized controlled trials in the field of prosthetics and orthotics. Other products were focused on preliminary analyses of partial data. A manuscript that covers the full data set and corresponding findings has been submitted to the Journal of Prosthetics & Orthotics. We will submit an abstract for consideration at the next applicable DoD conference (e.g., the 2021 Military Health System Research Symposium) as well.

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

A number of graduate assistants (Table 2) were supported through this grant and were gathering hands-on research experience by taking on duties in the context of executing the protocol. Those students received individual guidance and mentoring from the investigators, as well as standardized training in human subjects' protection and research ethics. They were able to incorporate their contributions to this project into their graduation deliverables as well and were leading some of the dissemination efforts by submitting conference abstracts based on aspects of the research.

Also, the unanticipated necessity to replace part of the study team led to some activities in the domain of training and professional development. PI Fiedler met repeatedly with colleagues and students at Widener University, in order to convey knowledge specific to this research area, including the state of the science, typical barriers and limitations, and the importance of the goals of this project in this context.

Finally, this project was the first of its scale and complexity to manage for PI Fiedler, which entailed ample opportunity for gaining pertinent experience in this aspect of academic endeavor. Both by design (e.g., the data collection being conducted at multiple sites) and by circumstance (e.g., unexpected changes in the core team and the natural environment), this project presented a host of challenges and lessons learned. Those experiences will be helpful for the further professional development as an effective PI in larger scale studies.

Table 2: Students participating in the project work

Student assistant	Level/University	Dates participating	Outcome
Zhang Xueyi	PhD/Pitt	Sep 2018-May 2019	Graduated in 2019
Danielle Sell	MS/Widener	Sep 2018-Mar 2020	Graduated in 2020
Robert Johnston	MS/Widener	Sep 2018-Jul 2020	Graduated in 2020
Kevin Quinn	MS/Pitt	Jun 2019-Apr 2020	Graduated in 2020

How were the results disseminated to communities of interest?

Following the unblinding after the conclusion of the data collection, participants were informed about their respective group allocation in order to enable them to change their regular liner prescription according to their preference.

Planned avenues for dissemination of results to members of the local target population included the annual "Spring Amputee Event", organized by DeLaTorre Orthotics & Prosthetics, various monthly support group meetings in the Pittsburgh region, and Events at the Homestead Community Engagement Center that is partly sponsored by the Pitt

School of Health and Rehabilitation Sciences. Those channels had been utilized for recruitment purposes earlier. Restrictions on in-person meetings and associated logistical challenges have led to cancellations and/or postponements of the respective events in recent months, so that the planned presentations will take place at a later time.

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

Nothing to Report.

IMPACT*:*

What was the impact on the development of the principal discipline(s) of the project?

The detected effect of the intervention on the assessed outcome measures was potentially clinically meaningful, suggesting that PCM liner use can reduce days in which patients do not use their prosthesis by about 12 per cent (from 19.0 days per year to 16.8 days per year on average). This information may be considered by physicians and practitioners when prescribing liner materials in the future. However, given that the study findings did not reach the pre-defined criteria for statistically significance, the impact on the development of evidence-based practices in the discipline of limb prosthetics is likely limited.

The major contribution of this work is therefore the development of a feasible double-blinded randomized control trial protocol to investigate prosthetic & orthotic interventions. This addresses a noted shortcoming in the arsenal of research tools in the discipline, and the respective journal publication has met with encouraging resonance. It is anticipated that future research studies across the prosthetics & orthotics discipline are impacted by this groundwork. The PIs have already gone on to apply the basic principles of the published protocol to new research studies (e.g., a funding proposal, submitted to the CDMRP mechanism in 2019, to investigate the long-term outcomes of different lower limb exoskeletons/orthoses).

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

According to the aims of the study, findings were expected to inform the prescription of prosthetic liners based on the used materials. This would impact the transfer of new technology, such as the tested phase change material liners into clinical practice. Given the inconclusive results of our analysis, this impact will be smaller than expected. Assuming that the developed protocol is adopted for future studies of innovative socket comfort interventions, this will help generate clinical evidence to enhance transfer of such technology as appropriate.

What was the impact on society beyond science and technology?

Nothing to Report.

CHANGES/PROBLEMS:

Changes in approach and reasons for change

A major problem for the data collection was the Covid-19 pandemic in the last year of the project period. The nature of the study that was designed to collect realistic long-term outcome data over two consecutive 6-month periods was incompatible with any reasonable changes that could have been undertaken to account for the impact of the pandemic and the associated mitigation efforts. Most notably, the long-lasting mandates of social distancing and the rapid economic decline during the pandemic have inevitably affected our participants' activity levels and thereby the main outcomes of the study to a much larger extent than the mere change of liner material (i.e., the study intervention) was hypothesized to do. In the early days of the pandemic, when the duration and severity of the restrictions was not yet fully predictable, the data collection was paused in accordance with applicable regulations by the Human Subjects protection offices. This temporary suspension eventually became permanent as the prescribed study period expired in the summer of 2020. The resulting shortfall in data posed the issue of an insufficient sample size for the planned analyses.

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

The above-mentioned impact of the pandemic response on the study was amplified as a result of earlier problems in the study period that affected the timeline of this project and led to the circumstance that data collection for a substantial portion of the sample was still ongoing in early 2020.

The unexpected passing of Widener site-PI Akins early on in the project period (February 2018) and subsequent challenges in replacing him in the study team had, among other things, affected recruitment at the Widener site and resulted in a shortfall of participants. We took advantage of a no-cost extension and developed plans for the enrolment of a third participant cohort in an effort to still achieve the target sample size before the end of the project period.

Even before the pandemic, recruitment and retention rates of participants proved to be lower than anticipated. It had been assumed that the nature of the study which had a low burden of participation (simple intervention that does not require changes to normal routines, conveniently scheduled and well compensated follow-up appointments, non-invasive data collection procedures, free study liners to cover a year of supplies) would make it attractive, and make it likely for participants to sign up for and complete even the year-long study. However, a combination of many potential participants being ineligible according to our exclusion criteria, unexpected fitting issues during the study period, and limited enthusiasm about the study among some local prosthetists challenged those assumptions. We increased our recruitment efforts, adjusted inclusion criteria (expanding from only trans-tibial to also include trans-femoral prosthesis users), and shortened the intervention period (from 12 to four

months) for the planned third cohort in an effort to evaluate the comparative effectiveness of such a streamlined protocol. This plan was frustrated by the pandemic as well.

Changes that had a significant impact on expenditures

The above-mentioned changes to the timeline entailed delays in staffing for this study and the unexpected personnel changes necessitated additional preparations, logistics, and training activities. The associated expenses were offset by the lower expenditures for participant compensation and follow-up due to part of the sample not finishing the entire protocol.

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

No changes to report.

Significant changes in use or care of human subjects

No changes to report.

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

PRODUCTS:

Publications, conference papers, and presentations

Journal publication:

Fiedler, G., Singh, A., Zhang, X. (2020) "Effect of temperature control liner materials on long term outcomes of prosthesis use, A Randomized Control Trial Protocol", Trials, 21/61 doi: 10.1186/s13063-019-3920-4

Fiedler, G., Singh, A., McKernan, G. (forthcoming) "Does socket liner material impact clinical outcomes in lower limb prosthesis users? Insights from a randomized control trial", Prosthetics and Orthotics International, under review

Books or other non-periodical, one-time publications:

Johnston, R., (2020). "Effect of Temperature Control Liner Materials on Long Term Outcome of Prosthesis Use", Master's Thesis, Widener University School of Engineering. July 2020

Sell, D., (2020). "The Effect of Different Liner Materials on Gait Mechanics in Transtibial Amputees", Master's Thesis, Widener University School of Engineering. March 2020

Other publications, conference papers, and presentations.

Fiedler, G., Singh, A., Zigler, C. (2019). "Applicability of Double-Blinded Randomized Controlled Trials in Prosthetics & Orthotics Research", 45th Annual AAOP Meeting and Scientific Symposium, Orlando, FL, Mar 6-9

Fiedler, G., Singh, A., McKernan, G., Zhang, X. (2019). "Effect of Liner Material on Prosthesis User Activity – Preliminary Data", American Orthotic and Prosthetic Association (AOPA) Assembly, San Diego, CA, Sep 25-28

Johnston, R., Sell, D., Fiedler, G., Peters, J., Singh, A. (2020). "Effect Of Temperature Control Prosthesis Liners On Gait Speed And Activity Levels Of People With Lower Limb Loss". Virtual Summer Biomechanics, Bioengineering and Biotransport Conference (SB3C), June 17-20

Website(s) or other Internet site(s)

Pitt+Me study page: https://pittplusme.org/studyarms/publicdetails?guid=321eea6d-40c0-4cae-87f2-2e6a7e4ae34b

Clinicaltrials.gov page: https://clinicaltrials.gov/ct2/show/NCT03428815

Technologies or techniques

Nothing to report.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Nothing to report.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	*Goeran Fiedler*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	*Gfiedler*
Nearest person month worked:	*10*
Contribution to Project:	*IRB compliance, recruitment/ enrollment of subjects, visit/training at Widener site, data interpretation/dissemination, reporting*
Funding Support:	

Name:	*Jonathan Akins*
Project Role:	*Co-PI (through Feb 2018)*
Researcher Identifier (e.g. ORCID ID):	*jsakins*
Nearest person month worked:	*2*
Contribution to Project:	*Study preparation and oversight at Widener site, IRB application and protocol modifications, preparation for recruitment, GSR hiring*
Funding Support:	

Name:	*Zhongping Huang*
Project Role:	*Co-PI (Mar - Jul 2018)*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*0*
Contribution to Project:	*n/a*
Funding Support:	

Name:	*Anita Singh (from Aug 2018)*
Project Role:	*Co-PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*5*
Contribution to Project:	*IRB compliance, recruitment, GSR hiring and training, supervision of data collection, dissemination*
Funding Support:	

Name:	*James Peters*
Project Role:	*Co-investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*data collection, recruitment and screening, scheduling, supervision of student assistants*
Funding Support:	

Name:	*Xueyi Zhang*
Project Role:	*Graduate research assistant*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*8*
Contribution to Project:	*Training, participant scheduling, data collection, post-processing, dissemination*
Funding Support:	

Name:	*Kevin Quinn*
Project Role:	*Student research assistant*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*Training, protocol review, manuscript development, assistance with recruitment, screening, and material ordering*
Funding Support:	

Name:	*Robert Johnston*
Project Role:	*Student research assistant*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*Data collection, assistance with recruitment, screening, scheduling*
Funding Support:	

Name:	*Danielle Sell*
Project Role:	*Student research assistant*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*Data collection, assistance with recruitment, screening, scheduling*
Funding Support:	

Name:	*Gina McKernan*
Project Role:	*Statistician*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Executing the blinding protocol, processing and analysis of preliminary data*
Funding Support:	

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

No.

What other organizations were involved as partners?

Organization Name: *Widener University*

Location of Organization: *Chester, PA*

Partner's contribution to the project: *Recruitment, data collection, secondary analysis, dissemination, (collaboration as external site for this multi-site study)*

SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: *An updated Quad Chart is included with attachments.*

APPENDIX: *Submitted manuscript, currently under consideration for publication at Prosthetics and Orthotics International*

Does socket liner material impact clinical outcomes in lower limb prosthesis users? Insights from a randomized control trial

Goeran Fiedler, Anita Singh, Gina McKernan

Abstract: *Among the noted disadvantages of prosthesis suspension by flexible liner is the increased rate of perspiration within the socket, which has the potential to cause discomfort, suspension issues, and tissue damage. In recent years, phase-change material technology has been adopted for the use in prosthesis liners, in an effort to improve temperature control and, consequently, reduce sweating. Previous work has demonstrated that this approach is effective in slowing the temperature increase at the limb-socket interface but it was not clear how this would translate to clinical outcomes. Therefore, the here presented study had the aim to compare conventional and phase change material liners with regard to prosthesis utilization, physical performance, and patient-reported outcome measures. A randomized double-blind cross-over study design with six-month intervention periods was utilized. Of the 42 enrolled participants, only 50% completed the protocol, owing in large part to the Covid-19 pandemic that started disrupting daily life and thereby the data collection midway through the study period. Findings indicate that the temperature control liners were, by trend, associated with better prosthesis utilization. The found effects did not reach the level of statistical significance, which is likely a result of the unduly reduced sample size.*

Keywords: *prosthesis liner suspension, socket comfort, temperature control, prosthesis utilization, phase-change material*

Background

The multitude of secondary health challenges that accompany lower limb loss is well documented. Among other things, common aftereffects of a limb amputation include muscle atrophies (1), restricted range of joint motion (2), blood circulation issues (3), and greater fall risks (4). Prostheses are generally prescribed to facilitate bipedal locomotion, which improves social participation and mitigates some of the long-term side effects of a sedentary life style. Active prosthesis use requires a reliable coupling between residual and artificial limb, which, in the case of conventional socket prosthesis, is realized by a tight fit of the individually customized socket, often utilizing a liner suspension system. Roll-on liners provide superior suspension and have become the de-facto standard of care in lower limb prosthetics after they were introduced in the 1980's (5). However, they are associated with various side effects that are mostly rooted in the inherent sustained contact with a large area of the residual limb surface. Many users report increased sweating, which requires them to frequently doff and dry their liners. Beyond the acute discomfort it can cause, the sweat accumulation also holds the risk of suspension loss, which may lead to accidental falls, and of increased friction, which can result in skin damage over the longer term (6-9). Importantly, any skin breakdown, even if apparently minor in nature, should be considered a significant concern, as it can prohibit the user from utilizing the prosthesis as intended and can thus be potentially as disabling as a much more severe injury after a fall. Prosthesis users are advised to closely monitor the skin health of their residual limb and to allow for emerging skin sores to completely heal before resuming prosthesis use again. In many cases, this recommendation entails frequent periods of limited mobility, which have adverse implications for social participation, employment, and psychological health (10).

One of the proposed approaches to the sweating problem is to moderate the climate at the skin-liner interface by adopting modern phase-change materials (PCMs) for use in prosthesis liners. PCMs are designed to absorb some amount of thermal energy by changing between solid and liquid phase at a designated threshold, which can help steady the temperature of the material even when ambient temperature changes. Previous work has demonstrated that, during the same physical activity, socket temperature and perspiration rose slower in PCM-based liners than in comparable conventional liners (11). In order to investigate whether those effects yield sustainable clinical (12) and, by extension, economical (13) benefits, the here presented longer-term study was initiated. It was hypothesized that lower perspiration results in improved prosthesis utilization (i.e., a lower number of days in which the prosthesis is not worn), following the rationale that less sweating results in less skin damage and less downtime to facilitate recovery. Secondary hypotheses were that physical performance and patient-reported quality of life (14, 15) would be positively affected by the use of PCM liners. Additional goals of the study were to identify potentially unexpected long-term effects of the liner intervention and to generate a template for future randomized control trial protocols in the research area of socket comfort.

Methods

The study protocol was reviewed and approved by the human subjects protection offices at the participating institutions and the study sponsor.

Participants who had a lower limb prosthesis with liner suspension, an activity level of K3 or higher, and no current skin health problems were recruited, screened for eligibility, and enrolled after providing informed written consent. Exclusion criteria were the use of a non-standard liner size and any known allergies against liner materials. The target sample size was 50, which allowed for an 18% (n=9) attrition rate to achieve a statistical power of 80%.

For each participant a total of four study liners was ordered. Two liners, representing the intervention condition, were from PCM (“Smarttemp”, Ohio Willow Wood Company, Sterling, OH) and two liners from conventional silicone gel material, representing the control condition, were custom-made to look identical to the intervention liners.

The one-year data collection period, beginning with the first set of liners being provided to the participants, was timed to commence in the month of January or July in order have the two six-month intervention periods cover a similar seasonal temperature cross section that included both the coldest and warmest months of the year. The sequence in which individual participants received their sets of liners was randomized, and the indistinguishable design of the study liners effectively blinded both participants and study prosthetists to the respective group allocation. At the six-month mark, the second set of liners was provided to complete the cross-over protocol.

An activity monitor (Stepwatch, Modus Health, Washington, DC) was affixed to each participant’s prosthesis and daily step count data was read out during frequent follow-up appointments throughout the study period. In six-weekly periods, participants were asked to complete a Prosthesis Evaluation Questionnaire(PEQ) (16), a PLUS-M survey (17), and a Two-minute Walk Test (18).

Data analysis included descriptive statistics as well as non-parametric comparison of the outcome variables “Days without prosthesis use”, “Average daily step counts”, “PEQ subscale score”, and “Two-

minute walk distance" across the two liner conditions at the end of each intervention period. A significance criterion of α=0.05 was applied.

A detailed description of the protocol has been published previously (19).

Results

A total of 42 participants were enrolled of whom only a subset completed the protocol before study activities were disrupted by the Covid-19 pandemic in early 2020. Disregarding participants who dropped out before the cross-over mark or who did not comply with the protocol left a final sample of 21. Participants in the included sample were on average 58 years old (standard deviation (SD) 8 years), at a height of 177 cm (SD 11 cm), and a body weight of 99 kg (SD 26 kg). At the beginning of the study, they had been living with limb loss for an average of eight years (SD 11 years) and their mobility rating, measured by the PLUS-M survey, was on average in the 73th percentile (range 30th to 95th percentile) of the overall lower limb loss population.

None of the found differences in any of the outcome variables (Table 1) were significant at the 0.05 level.

Table 3: Averaged outcomes of the two liner types. 2MWT - Two-minute walk test distances, PEQ - Prosthesis Evaluation Questionnaire (sub-sections)

Variable	PCM liner	regular liner	relative difference/%
% prosthesis utilization	95.4	94.8	0.6
2MWT (m)	98.3	99.6	-1.3
PEQ subscales (in % of max score)			
Ambulation	75.0	69.5	5.5
Appearance	80.8	81.8	-1.0
Health	71.9	67.9	4.0
Sounds	85.7	89.7	-4.0
Utility	73.9	71.5	2.3
Wellbeing	68.2	70.9	-2.7

Discussion

The available data did not support our hypotheses that PCM liners had significant benefits for prosthesis utilization, physical performance, or prosthesis-related quality of life. This finding must be interpreted in light of the sample size limitations that prevented conclusive results. However, while a larger sample, as initially planned, might indeed have yielded statistical significance, it is already apparent that the effect sizes for many of the investigated outcome variables are generally small. This is consistent with earlier findings that the (statistically significant) reduction in skin temperature when using PCM liners did not exceed 0.8 °C (11). Nominally small effects can still be clinically significant. For example, the found difference in prosthesis utilization represents an annualized rate of 2.2 fewer days in which the artificial limb was not worn. While apparently a minor improvement, this can translate into relevant outcomes when those days are used for gainful employment or to attend business or private events that are important to the individual.

The previously reported minimal clinically important difference recorded in the mobility subscale of the PEQ is 16.5% of the maximum score (20), which suggests that the respective differences between liners in our study, of 5.5% or less, are negligible. That no consistent trend among sub-scales is recognizable is in line with the likely random nature of those differences.

Even though this study did not yield the hoped-for conclusive results, it may provide some useful insights about the feasibility of a double-blind randomized control trial of prosthetic interventions. Comparing liner materials offers the unique opportunity to employ a placebo with effective concealment of the group allocation both to the participant and the study personnel (apart from one individual who is responsible for the randomization protocol and is not otherwise involved in study procedures). The length of the intervention periods of six months for either condition was selected to make the protocol most representative of real-life conditions while still enabling a cross-over design without a marked baseline drift. An 18% attrition rate was anticipated, which proved too optimistic when 25% of the 20-person first cohort dropped out due to various fitting issues alone. Technical issues (prosthesis damage) and unrelated health issues further decimated the sample, and the emergence of the worldwide Covid-19 pandemic effectively ended the data collection before the 22-person second cohort could complete (and the planned third cohort could even begin) the protocol.

Randomized control trials are important to strengthen the evidence base in prosthetics and orthotics. Our experiences suggest that intervention periods for such trials should be limited as much as reasonable. Future studies on the effectiveness of socket temperature control interventions, for instance, may be best scheduled for a period that covers only the summer months where the investigated effects are likely most pronounced.

Acknowledgment
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