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Inclusivity in Combat Amputee Research: An Analysis of Underrepresented Populations

Victoria Eichorn

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INCLUSIVITY IN COMBAT AMPUTEE RESEARCH: AN ANALYSIS OF UNDERREPRESENTED POPULATIONS

by

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A Thesis Submitted in Partial Fulfillment of the Requirements for a Degree with Honors (Biology)

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ABSTRACT

Females and minorities are two underrepresented communities in a multitude of areas. The two areas that are of interest to this paper are: clinical research and the military. The female population, in particular, was examined because of two policy changes that took place in 2016: the lift of the ban on females in combat positions and the requirement that sex be investigated as a biological variable in scientific research. Therefore, one focus of this study was to examine whether these policy changes led to increased representation of women. Lacking access to databases containing the data of interest, a modified meta-analysis approach was completed. In this study, three databases and archives were used to collect data which was then refined with inclusion/exclusion criteria. The search through the databases and archives yielded a total of 72 datapoints (articles) that met the criteria. From these datapoints, it was determined that the results supported the hypothesis that the collected information would not accurately represent the female population. The results of particular interest within the findings were basic demographic data (sex ratios and race/ethnicity inclusion), publishing dates, military status, amputation types, and affiliations of articles. Of the 72 datapoints, 43% included females in their populations, 38% did not report sex of subjects, and 19% used only male subjects. In terms of other demographic results, 12.5% reported more than two races, neither military status nor amputation type was found to be a prevalent factor included in the articles, and most studies were affiliated with the military. These results are important to take into consideration because of how they can apply to female combat amputees seeking prosthetics or medical treatment, as well as examining how the addition of
inclusive policies in communities like the military or that of clinical research truly affect
the treatment of females and underrepresented populations within these communities.
ACKNOWLEDGEMENTS

I would like to thank my advisor, Lynn Atkins, for all that she helped me through. Her guidance and her humor made this entire process much more enjoyable than I had initially expected. I would also like to thank my committee members, Dr. Margaret Killinger and Dr. Jennifer Blossom, both of whom kindly shared their time, resources, and expertise.
TABLE OF CONTENTS

INTRODUCTION 1

BACKGROUND 2

Females and Minorities in Science 3

Women and Minorities in the Military 10

METHODOLOGY 13

RESULTS 17

DISCUSSION 22

CONCLUSION 33

REFERENCES 35

AUTHOR’S BIOGRAPHY 47
LIST OF TABLES, FIGURES, AND DEFINITIONS

Definition 1: “sex(es)” 2
Definition 2: “combat amputee” 3
Table 1: Search Terms 14
Table 2: Extracted Data 15
Table 3: Articles Including Females and more than 2 Races/Ethnicities 17
Table 4: Demographic Ratios of Pooled Article Subjects 18
Figure 1: Publication Timeline 18
Figure 2: Military Status 19
Figure 3: Amputation Type 20
Figure 4: Affiliations 21
Figure 5: Pooled Population Sex Proportions 21
INTRODUCTION

For this study, females were the particular subject group of interest, more specifically examining female representation in combat amputee research. Thus, the research question was: How have policy changes governing scientific research and military operations affected combat amputee research with regard to the inclusion/representation of females? However, during the course of collecting data, other groups were found to be underrepresented as well (i.e. races or ethnicities other than white and trans- or non-binary gender individuals). Therefore, the primary interest of this study examines the female population, however minority subjects were also examined as a sub-interest. This determination was made due to the applicability of both 2016 policy changes that occurred in the clinical research and military communities to females. Hence, the majority of the background information and analyses that were conducted relate to females. Thus, the hypothesis for this research is as follows: due to the historical exclusion of females in combat and in clinical research, it is theorized that the data will not accurately reflect the female population.
BACKGROUND

Anatomically, physiologically, psychologically, and socially, we know that males and females are different. However, the evidence of this fact has not been reflected in clinical research until relatively recently. Even still, examining the entirety of sex differences in scientific literature was an incredibly broad research topic. For the purposes of this study, the term “sexes” refers to males and females. While gender is a spectrum, this research looks at the biological differences between males and females to assess appropriate medical treatment. Non-binary and trans individuals were included within the parameters of this study, however, none were identified within the pooled subject population.

The second community of interest for this examination is that of the United States (U.S.) military. In terms of war or conflict, we know that it has existed for as long as anyone can remember. Yet, the legal inclusion of women in combat is a recent change to policy made by the U.S. military. Even the classification of “in combat” has been, and continues to be, debated. This debate still occurs because women have been in combat zones as medical professionals and other field occupations, but were not legally allowed to join military combat teams. Those that were in combat when the ban was still in place were not appropriately recognized.

Despite the marginalization of women in both the scientific community and the military, research on the difference in treatment between the sexes within the context of these communities was still an incredibly broad topic to study. Hence, the aim of this research was to explore females in combat amputee research, with the hypothesis that the data would not accurately reflect the female population due to the historical exclusion of
these populations. Incorporating the condition that subjects must be combat amputees greatly reduced the scope of the study so that the larger sociocultural impacts could be analyzed as well as multiple marginalized demographics. One important thing to note is the phrase “combat amputee”. This phrase was used by most, if not all, articles, however the way that each article defined the phrase varied slightly. In general, the definition was an individual with a traumatic amputation(s) that was conducted in the field.

**Females and Minorities in Science**

The history of female and minority inclusion in clinical research in the United States is a tumultuous one. Starting in the 1970s, official recommendations for female-excluding policies regarding pharmaceutical research subjects took effect. Prior to these changes, many researchers assumed that the effects of their experiments would be the same with both males and females, thereby only testing treatments on males. Hence, female inclusion in experimentation was not prioritized. This led to a lack of medical information for women, and resulted in detrimental effects on the female population.

In the 1950s and 60s, thalidomide was often used to ease nausea in pregnant women (53). However, it was later found that pregnant women who used thalidomide gave birth to children with life-threatening deficits (21). Thus, in 1977 the Food and Drug Administration (FDA) recommended researchers implement a policy that would exclude women from Phase I and early Phase II of drug trials until reproductive toxicity studies had been conducted. The reasoning provided for this policy was that it was meant to protect potential childbearing women (33). However, this policy resulted in the exclusion of women that were using contraception, single women, and women whose husbands had
had vasectomies. Therefore, the recommendation of this policy also led to a considerable lack of data on how pharmaceuticals affected females.

Later, in 1987, the National Institute of Health (NIH) published a policy that encouraged researchers to include females in studies. This policy was later edited in 1989 to encourage the inclusion of women and minorities in research solicitations. This memorandum also stated that if women or minorities were to be excluded, a rationale was required. In theory, this policy change should have affected how research was conducted and underrepresented populations should have had more representation moving forward. However, in a Government Accountability Office (GAO) investigation conducted in 1990, it was found that these recommendations had fallen short. The findings cited that the communication of the policy was lacking, application was inconsistent, and the analysis of data by sex had not been sufficiently encouraged by the NIH. Thus, medical treatment for underrepresented populations, which depends upon clinical research, would have no chance to change in order to suit the needs of the populations that were not represented.

To account for this error, two months after the investigation’s findings, the NIH implemented the Office of Research on Women’s Health (ORWH) with the purpose of monitoring inclusion. To further encourage female-inclusion, in 1991 the first female director of the NIH created the Women’s Health Initiative which was designed to focus research on ways to prevent breast cancer, cardiovascular diseases, and fractures from osteoporosis (49). This effort was rewarded in 1993 when Congress made the female and minority inclusion policy, created by the NIH, a Federal law. In the same year, the FDA repealed the 1977 recommendation and instead established a guideline recognizing the
importance of testing pharmaceutical effects on different populations. The tradeoff was requiring that participants be sufficiently informed in order to give educated consent to whatever they were taking part in. Although these regulations highlight the history of women in pharmaceutical research, the same exclusionary perspective was adopted throughout the clinical research community.

Evidence of female exclusion dominating the field of clinical research is shown in studies conducted on animal subjects (20). While they do not involve human females, these studies are relevant to the argument because many researchers use model organisms that humans share traits with to limit human subjects’ research. This methodology is still used today because animal subjects limit ethical concerns with human subjects’ research, while providing accurate information on human health concerns. Therefore, if female animals are not subjects in analog studies, the researchers have no frame of reference for how their experiments affect women. A study conducted by scholars at Stanford stated that while the requirement of female and minority subjects in research made by the NIH makes sure to include these populations in human subjects’ research, it does not apply to animal subjects research. This policy also only applied to NIH-funded clinical research (20). Prior to the requirement issued by the NIH, sexes of animal subjects were rarely reported, and even with the NIH requirement in place, “22-42% of articles in neuroscience, physiology, and interdisciplinary biology journals” did not report the sex of their subjects (6). This omission creates issues for the female population, as it results in inaccurate health information (4). Finally, in 2016, the NIH established sex as a biological variable to be factored into both human and animal studies, and those that do not incorporate sex as a variable are required to provide reasoning (102).
Despite their known biological differences from males, females were overlooked in clinical research because of the assumption that treatments will have the same effects on females as they do on males. Similarly, minority populations were neglected because of a white-centered mindset. The seriousness of this neglect cannot be understated because there are enormous amounts of data supporting the claim that females have substantial biological differences compared to males, as well as overwhelming evidence of different genetic predispositions between races/ethnicities. Some of the most relevant biological sex and racial/ethnic differences related to amputee health are: gait kinesiology, muscle architecture/distribution, pain response, and hormonal impact on immune response, aging, as well as disease.

The relevance of the listed overall biological differences lies in their impact on day to day life. For instance, gait kinesiology and muscle distribution/architecture largely affects walking and running. The findings of Bruening et al and Bartolomei et al respectively, show that females have greater range of motion than males when it comes to gait and they have greater lean body mass. Whereas, male muscle distribution and architecture is thicker in their chest, upper back/neck/shoulders and thighs. Therefore, these biological differences should have an impact on how generalizations are made about most effective walking and running techniques or how treatments related to walking and running are determined. Yet, a lack of research in this area puts females at a huge disadvantage because it means that the techniques learned and courses of treatment administered are primarily suited for males, and thus not as effective for females.

Similarly, sex differences in pain response as well as hormonal impacts on immune response, aging, and disease affect day to day life as well. Supporting this
statement are studies with the following findings: females have a greater sensitivity to pain and hormones impact females at different ages (pre-menopause and post-menopause) completely differently than their male counterparts (7). Pre-menopausal females have better immune responses than males of the same age (55). However, post-menopausal females are almost immediately at higher risk of contracting neurodegenerative, neuro-vascular, and bone diseases than their male counterparts of the same age (65). By comparison, male hormones gradually deplete over time resulting in a gradual decline of effective immune response, muscle mass and bone density (79). This gradual decline seen in males is not seen in females due to the drastic change in hormone levels that are the result of menopause.

The implications of these differences for amputees can be interpreted from medical treatments. Since the standard of care is based off of a male-model, the major risk factors for females can be neglected and therefore have detrimental effects on female health. For instance, the higher risk in post-menopausal females of contracting neuro-vascular diseases means that they are at higher risk for blood flow issues, particularly to the brain and spine. Since the most common reason for amputation is vascular issues (54%), the higher risk in post-menopausal females should be recognized by physicians and clinicians. Other implications for amputees in terms of post-menopausal females at higher risk for bone diseases and decreased bone density which can be particularly difficult for amputees. Decreased bone density results in fractures, which occur due to different kinds of stressors on the bone. Treatment of fractures in amputees have been found to be challenging due to the altered anatomy (74). Cited challenges include: diagnosis, immobilization, stabilization, and rehabilitation.
Along a similar line, different genetic predispositions between races/ethnicities result in unspecialized and uninformed medical care. For instance, the prevalence of Peripheral Artery Disease in black individuals, which occurs three times as often in black individuals than in white. Another example is the prevalence of diabetes diagnoses among different races/ethnicities: 14.5% American Indians/Alaskan Natives, 12.1% non-Hispanic Black individuals, 11.8% Hispanic individuals, 9.5% Asian Americans, and 7.4% non-Hispanic white individuals (1). Despite these major differences, white males have still been studied to a greater extent than females or minority populations, resulting in less information on how these aspects of daily life affect them biologically.

All of these examples provide evidence of drastic biological differences between males, females, and different races/ethnicities. However, they also focus on major biological features that factor into day to day life for amputees. Amputations drastically alter how an individual functions, and if the medical community is not aware of how their treatments and procedures effect females versus males or white versus minority races/ethnicities due to a lack of data, that puts female and minority patients at an enormous disadvantage. Not only do the sex and race/ethnic differences impact medical treatment of amputees in general, they also impact amputees that choose to use prosthetics. In particular, gait kinesiology, muscle architecture/distribution, and genetic predispositions largely affect how prosthetics are made and used. However, sex and race/ethnic differences in genetics, pain response, and hormones should also impact how the prosthetics change over time. Since females are predisposed to neurodegenerative, neuro-vascular, and bone diseases, adaptions to treatment should be made to better benefit them. In terms of races/ethnicities, symptoms of genetic predispositions should be
examined more thoroughly, such a diabetic symptoms in minority groups to prevent further health concerns. These populations perceive pain differently, age differently, and have different susceptibilities, all of which influence functionality and use of prosthetics.

To contextualize the proportion amputees in the United States, according to the Amputee Coalition, almost 2 million people in the United States are living with limb loss out of approximately 332 million people total. While amputees compose an admittedly small proportion of the total people in the U.S., treatment and care for amputees differs drastically from that of the non-amputee population. In looking at the main causes for amputation, they are vascular disease (54%), trauma (45%) and cancer (<2%). The subject population of this paper fall into the category of trauma, as they are amputations that have occurred within the combat field. However, these population proportions are not static, studies cited by the Amputee Coalition predict the number of amputees in the U.S. to be closer to 3.6 million by 2050. Hence, the importance of research regarding amputees will, in theory, increase as the amputee population increases.

With regard to demographic proportions, as of 2014, male amputation patients comprised 69% of amputees and 31% of amputees were female. This means, within this already small portion of Americans that are amputees, an even smaller portion are female. The small population size of female amputees, or any other minority group, can lead to researchers omitting sex as a biological variable in their research because of their lack of size as a population. Additionally, in the U.S., black individuals are 4 times more likely to have an amputation compared to white individuals. Latinx individuals are 1.5 times more likely to have an amputation than white individuals and Indigenous individuals can be up to 70% more likely to have an amputation compared to insured,
non-indigenous, adult individuals (2). Also stated by the Amputee Coalition, the frequency of lower limb amputation is at 65% compared to upper limb amputations at 35%. Similar to sex statistics, this statistic on amputation types can result in research that only focuses on lower limb amputees because of the larger population. Finally, according to the United States Department of Health and Human Services, of all military personnel that were in Afghanistan or Iraq, 1,558 lost a limb as a result of the wars (103).

Given all of this information regarding female and minority history with clinical research, the distinct biological differences between sexes and races/ethnicities, as well as the proportions of amputees in the U.S., one can easily come to the conclusion that females and minorities have been underrepresented in clinical research.

**Women and Minorities in the Military**

As with females and minorities in clinical research, the history of demographic diversity in the military is quite chaotic. All of the following dates will be of legal changes to policy which do not necessarily reflect the participatory practices of individuals accurately. Starting with the desegregation of the armed forces, non-white races or ethnicities were legally allowed to participate in combat as of July of 1948 (75). Also in 1948, women were legally granted the ability to serve in all branches of the military. However, women were not allowed to serve in all combat positions until 2016 (81). Also in 2016, the Secretary of Defense determined that trans individuals can and should be included in the armed forces. Despite this conclusion, it was not legalized until January of 2021 that individuals of any identity were allowed to serve openly (12).
In reality, individuals of racial and ethnic minorities, women, and the trans community have served in the military and combat positions prior to any executive order or policy change. Examples of this are the Tuskegee Airmen: a group of primarily black fighter pilots who fought in World War II (99); Margaret Corbin: a woman who dressed as a man and fought on the front lines of the Revolutionary War with her husband (23); and Albert Cashier: originally born in Ireland as Jennie Hodgers (45). Albert immigrated to the U.S. and enlisted in the army as a man at 18, after the war they continued to identify as a man and was never questioned until a car crash that outed them in 1911.

In terms of demographic percentages, according to the 2021 Department of Defense Military Demographic Report, 81.1% of total military personnel were male and 18.9% were female. With regard to race, 70.5% were white, 16.9% were black or African American, 4.9% were Asian, 3.2% were unknown, 2.6% were mixed, 1.1% were Native Hawaiian/Other Pacific Islander, and 1.0% were American Indian/Alaskan Native. The report also stated that 16.6% of total military personnel were ethnically Hispanic or Latinx (22). The numbers being what they are, one must also consider that these percentages account for all members, not just women or minorities in combat positions.

There has been much debate over whether or not women should be allowed in all combat positions; some points of view believe that women do not have the skills or anatomy necessary to be most effective in combative positions. Whereas, others argue that while women are not anatomically identical to men, this should not prevent them from serving in combat roles. With regard to this debate, studies have shown that if females and males in the military are presented with the same task, they are both able to complete it with the same results (35). However, the methodology differs between the
sexes. When males and females were told to complete the same task the same way (in a way that had been optimized for males), the female results could not compete. What this study essentially found was that even when it comes to the way the sexes approach a situation is inherently different. Thus, in a system optimized for male success, of course females are going to appear as though they cannot achieve the same standards as males.

Thus, different methodologies are required for optimal results when it comes to males, females, and racial/ethnic minorities in areas such as military combat or scientific experimentation because of the inherent differences between the populations. In terms of this study, the primary focuses are the biological differences between the sexes as well as some biological differences between races/ethnicities because both military scenarios and scientific research have neglected these differences in the past. Therefore, given this information, it was hypothesized that the data collected would not accurately reflect the diversity of the population in terms of sex, gender, or race.
METHODOLOGY

The main methodological approach taken in this research was descriptive data mining via modified meta-analysis of articles relating to combat amputees. Thus, the data for this study was mined from accessible articles that had been published using combat amputee subjects and sorted using search parameters, eligibility requirements, and inclusion/exclusion criteria. The PRISMA 2020 checklist for meta-analyses and systematic reviews was followed as a loose format for this modified meta-analysis.

In terms of the determined eligibility requirements, the one of the utmost importance was the use of only peer-reviewed articles. This requirement was put in place to help mitigate potential issues from unreliable data. The other requirements for eligible articles were as follows: studies using U.S. military combat amputee subjects, studies conducted in the U.S., studies published within 20 years, and studies conducting primary research. Both the subject requirement and the location requirement were used to narrow the scope of the study, also so that only U.S. policies need be examined for the analysis. The age requirement of the article was intended to mitigate potential issues stemming from outdated data or information, while also providing a timeline to compare article publishing date and policy enactment. It was necessary for each included study to be primary research because the primary question of this thesis revolved around how females and minorities are treated in clinical research. Thus a systematic review or meta-analysis would not provide eligible data.

The following databases and archives were used to access primary research articles: University Resources Serving Users Statewide (URSUS), the Journal of Rehabilitation Research and Development (JRRD), and the Association of Military
Surgeons of the United States (AMSUS). The URSUS database provided access to articles within the databases and journals of: PubMed, ScienceDirect, Taylor & Francis Online, Springer Link, Sigma, GALE, Wiley Online Library, and the International Journal of the Care of the Injured.

Following the determination of sources for data collection, the data was meticulously collected and recorded from each eligible article. Articles were deemed eligible if they adhered to the following inclusion criteria: published within the last 20 years, used U.S. Military combat amputees as subjects, conducted within the U.S., peer reviewed, and primary research. The search terms used when looking for articles are listed in Table 1 and filters excluding the following characteristics were used: articles 20+ years old, non-peer reviewed articles, news articles, and case studies. In the JRRD archive, the topics explored were: Amputation, Orthopedics, Prosthetics, Pain/Pain Management, and Psychological Rehabilitation.

Table 1. Search Terms

<table>
<thead>
<tr>
<th>Search Terms</th>
<th>Search Terms</th>
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<tbody>
<tr>
<td>combat amputee</td>
<td>limb loss</td>
</tr>
<tr>
<td>combat limb loss</td>
<td>combat amputates service members</td>
</tr>
</tbody>
</table>

Table 1. The contents of this table include the words and phrases used in the search bars of the various databases searched.

A total of 72 articles were found eligible for this study. Studies were reviewed and deemed eligible if they met the criteria listed previously, oftentimes titles and abstracts would be reviewed as well as subject demographic tables. The following category headings were used to sort and keep account of the data: Link, Number of Individuals, Female, NB/Trans, Male, No Sex, Race/Ethnicity, Location, Affiliations, Published within 10 years, Published within 11-20 years, Date of Injury, Method,
Military Status, Amputation, Peer Reviewed, Full Article, and Database (Table 2). The data was collected between November 2022 and January 2023.

Table 2. Extracted Data

<table>
<thead>
<tr>
<th>Extracted Data</th>
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</thead>
<tbody>
<tr>
<td>Link</td>
</tr>
<tr>
<td>Number of Individuals</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>NB/Trans</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>No Sex</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>Location</td>
</tr>
<tr>
<td>Affiliations</td>
</tr>
</tbody>
</table>

Table 2. The contents of this table are the headings implemented in the GoogleSheet used to organize the collected data from each article.

In the Number of Individuals, Female, NB/Trans, and Male columns the numbers of subjects within the article applicable to each category were recorded from each article. Throughout the process, comments were made noting that for a few articles the subjects recorded was not the total number of subjects in the study, rather they were the subjects relevant to this study (i.e. number of combat amputee subjects). The No Sex, Published within 10 years, and Published within 11-20 years columns were marked if the article adhered to the specifications. In the Race/Ethnicity column the reported race/ethnicity of subjects was recorded. Similarly, the date ranges provided in each article were the input of the Date of Injury column, type of amputation in the Amputation column, reported affiliations in the Affiliations column, and reported military status of subjects in the Military Status column. If the information for the previously listed columns was not specified, “n/s” was entered. Post data-collection, it was determined that specific
publication year would be beneficial for this study, thus the 72 datapoints were reviewed and publication year recorded.
RESULTS

Of the 72 articles that were eligible for this study, 27 did not identify the sex of their subjects. No articles identified their subjects as non-binary or transgender, and only 13 articles identified the race or ethnicity of their subjects. Of these 13 articles, 9 presented more than two categories for race/ethnicity in their findings, and 7 articles included more than two races/ethnicities and females (Table 3). In terms of other article data, this study found only 8 articles (0.1%) that did not have military affiliations, 53 (73.6%) articles were published within the last 10 years, 28 (38.9%) articles identified their subjects’ military status as a mix (active, service members, and veterans), and the second most common amputation was lower extremity amputation, where the most common type was mixed (upper and/or lower extremities).

Table 3. Articles Including Females and more than 2 Races/Ethnicities

<table>
<thead>
<tr>
<th></th>
<th>Including Females</th>
<th>Including 2+ Races/Ethnicities</th>
<th>Female &amp; 2+ Races/Ethnicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=72 n (%)</td>
<td>31 (43)</td>
<td>9 (12.5)</td>
<td>7 (22.6)</td>
</tr>
</tbody>
</table>

Table 3. The table above displays a break down of the total number of articles with percentages used in this study separated by inclusion of females, two or more races/ethnicities, and both.

Of the pooled subject demographics data from all of the articles, there were 22,792 subjects total, 206 (0.9%) of which had been identified as female, 14,606 (64.1%) were reported as male and for 7,980 (35%) subjects sex was not reported (Table 4).
Table 4. Demographic Ratios of Pooled Article Subjects

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
<th>Not Specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 22,792 n(%)</td>
<td>206 (0.9)</td>
<td>14,606 (64.1)</td>
<td>7,980 (35)</td>
</tr>
</tbody>
</table>

Table 4. The above table exhibits the total number and percentages of subjects from all of the articles included in this study separated by sex, as well as the number of subjects whose sex was not specified.

As for the data related to the specific focus of this study, the relevant results can be seen when comparing all article publication dates to only female-inclusive publication dates, military status reported in all articles versus only female-inclusive articles, all reported subject amputation types to only female-inclusive amputation types, all article affiliations versus only female-inclusive affiliations, and pooled population sex proportions. In examining the publication data of Figure 1, no specific trends were found in comparing overall publications and those that included females in their population. However, there was a notable overall disparity between the quantity of all combat amputee articles and articles that included female subjects, particularly in 2013: 6, 2014: 8, and 2016: 6.

Figure 1. Publication Timeline

Figure 1. This graph represents a quantitative timeline of publication years for articles included in this study. The values shown in the bar graph are of articles published including female subjects compared to all articles published.
With regard to military status of subject populations, displayed in Figure 2, similar trends can be observed between overall article populations and female-inclusive article populations. However, there is still a large disparity between population sizes within the breakdown. One important result to note are the amount of articles that described their subject population military status as mixed. This amount is double the second largest status for both categories of article, which was not specified.

Figure 2. Military Status

![Military Status Chart](image)

Figure 2. This figure shows the difference between military status of subjects in all articles and articles that included female subjects. The statuses included are as follows: mix, not stated, veteran, active, and servicemember.

Like military status, common amputation types were also observed to follow a trend, seen in Figure 3. For all articles it was found that in both categories the second most common amputation type was found to be lower limb, which was second only to mixed amputation type. Whereas, the lowest two amputation types were observed as upper/lower limb and unilateral transtibial for all articles as well. Also similar to the
publication data and military status data, amputation type data showed a large quantitative disparity between all articles and female-inclusive ones.

*Figure 3. Amputation Type*

![Amputation Type Chart]

Figure 3. In this figure, the quantity of amputation type is shown with regard to all articles and articles that included female subjects. The following categories were identified: upper limb, upper and lower limb, mix excluding fingers and toes, transtibial, lower limb, mix, unilateral transtibial, not stated, and unilateral transfemoral.

Next examined, in Figure 4, was a comparison of article affiliations for all articles versus only female-inclusive articles. In both categories, the highest quantity of affiliations was with a military organization, followed by colleges/universities, the department of veterans’ affairs organizations, and other organizations. One interesting aspect of this data to note is the number of affiliations with departments of veteran affairs organizations is nearly equal between all articles and only female-inclusive articles. As opposed to the rest of the figure which shows the same kind of quantitative disparity that the previous figures had. To put this obvious quantitative disparity in subjects into
context, Figure 5 shows that overall sex proportions were 43% female-inclusive, 38% did not disclose sex, and 19% as only male subjects.

**Figure 4. Affiliations**

![Affiliations of Studies with Females and Overall](image)

Figure 4. The figure above shows the article affiliation trends and disparities between all articles and those that included female subjects. The affiliations examined are as follows: military, department of veteran affairs, colleges or universities, and other organizations.

**Figure 5. Pooled Population Sex Proportions**

![ARTICLE SEX PROPORTIONS](image)

Figure 5. In the above figure, the proportions of sex attributed to subjects by article is displayed for all of the articles reviewed in this study. The proportions include: articles using male subjects only, articles that included females in their subject population, and articles that did not include sex of subjects in their data.
DISCUSSION

To review, the proposed hypothesis for this study theorized that due to the historical exclusion of females and other minority groups in combat and in clinical research, the collected data would not accurately reflect the diversity of the population in terms of sex, gender, or race. The results of this study yielded 72 eligible articles used as the primary data points. From these 72 articles, data regarding subject demographics within the articles was carefully mined and meticulously recorded so that subject data could be reviewed and analyzed according to the interests of this study.

The first portion of the results to analyze is the overall article data. As previously mentioned, 27 articles did not identify sex for their subject population and 31 included females. While this portion of articles not reporting sex is less than half, it is more than a third of all articles. As for the number of articles including females, it is still less than half, but admittedly close to half. However, according to the recommendations put in place by the NIH, these articles should have given some kind of reasoning as to why they did not examine sex as a biological variable. Given the timeframe, this policy was still a recommendation at the time and not yet codified. Although, this recommendation had been put in place for almost a decade at the time of the earliest publication date. Presumably, a decade is enough time to adopt a new policy and yet the results do not show effective implementation. In terms of non-binary and trans individuals, the military policy change including these folks did not officially start until 2021, therefore it is more understandable that none of the articles identified non-binary or trans subjects.
In conducting a similar analysis of racial and ethnic results, only 13 (18%) of articles included race/ethnicity in their demographic reports, and 9 (12.5%) of studies reported more than two races/ethnicities. Even more articles did not report race in their demographic findings than those that did not report the sex of their subjects. Given that the policy recommending the inclusion of minorities took place at the same time as the sex inclusion recommendation, these results show that the policy change was not effective.

A distinction was made between listed race/ethnicity and two or more race/ethnicities listed because of how many articles included “white/caucasian” and a non-white category as the only two race/ethnicities listed. The significance of this distinction is important to consider because reports of subject race/ethnicity affects treatment just as much as identification of sex. Multiple studies have shown that certain races/ethnicities are predisposed to certain conditions, such as black/African American individuals and sickle cell anemia (19) or Native Americans and diabetes (1). If no more than two race/ethnicity categories are considered in demographic data, the research is ignoring potential implications of genetic predisposition.

To combine the analysis of females and of minority races/ethnicities, only 7 articles reported more than 2 races in their subject demographics, which also included females in their subject population. Despite females and non-white races/ethnicities composing a minority of the combat amputee population, 7 articles is not enough representation for these populations based on the demographic statistics about the amputee and military communities. An important factor to note is that this number of articles does not take into account the number of subjects that apply to these categories.
In theory, the females and minorities included in these 7 articles could be substantial, but they could also account for one person. Either way, it is still not enough.

Next, the pooled population demographics from all articles was examined. The calculated ratio of male to female subjects was 64:1, using standard rounding techniques. Comparing this ratio to the proportion of male to female among all amputees in the United States (69:31) as well as the rounded ratio of males to females in the military (82:18), the found range of males to females does not adhere to neither the expected amputee sex ratio, nor the expected military sex ratio. An important factor to remember in this comparison is that sex was not identified in 35% of subjects, this 35% could skew the ratio in either direction. However, the absence of identified sex still has an effect on combat amputees. Without this context of subject sex, the reader of this research does not know how the experiments affect males versus females, if there was a potential difference. In turn, the absence of this information affects how combat amputees are treated in the medical world or whichever field the research pertains to.

Another aspect of the results to examine is the timeline of publication of the studies. External factors such as elections, wars, and length of studies are all important to consider when looking at the publication data. For instance, the conflict in Afghanistan lasted from October 2001-August 2021 and the conflict in Iraq lasted from March 2003-December 2011. After these two conflicts, the U.S. has not been involved in any other major conflicts that would result in combat amputations, yet the majority (73.6%) of the articles were published in the last 10 years. In looking at the trend of publication, there was an initial increase in 2006-2008, which falls in 2009, then spikes in 2010. After this spike, number of publications fall again in 2011 and 2012. However, publications spike
again in 2013 and remain relatively consistent until 2018. There is another spike in 2019, and another blip in 2021, however the majority of publications were released from 2013-2017. The initial increase is 5-7 years after the start of the Afghanistan conflict, which could be due to the length of time that longitudinal studies take. The following increases in publications occur in roughly 5-year increments from the start of the Afghanistan conflict, which can be typical increments for longitudinal studies.

Another factor to consider are the laws implemented within this timeline. For instance, in 2016 a federal law was implemented by Congress that sex must be included as an analyzed biological factor, and if not, reasoning had to be given. Despite the studies published in 2016 having the second largest differential between studies including females and overall studies, the years following have had fewer large gaps between overall studies and female-inclusive ones. When thinking about the time difference between article submission date to publication date, as well as how long these kinds of studies take, the fact that studies published in 2016 having large sex differential makes sense.

The other law that would have a massive impact on these studies was the lift of the ban on women in combat that was enacted in 2016. This ban lift could also be a factor in the fewer large disparities. Although, 2016 was only 7 years ago therefore it is difficult to determine the actual impact these laws have had on research pertaining to female combat amputees. Within the consideration of the law, the impact of the executive branch and politics as a whole on scientific research must also be examined. For example, George W. Bush served as president from January 2001-January 2009. In his terms, he promoted some medical and technological advancements, however he primarily had other
focuses. After that, Barack Obama’s term lasted from January 2009-January 2017. During his term, Obama promoted education and research in STEM fields, making this one of his priorities (76). The president after Obama served from January 2017-January 2021 and was generally uninterested in the advancement of scientific research. In this term, Congress expressed more interest in scientific advancement than the president (101). Following this, Joe Biden started his term in January 2021, and has announced various advancements in science policies looking to improve open and equitable research (100). Aligning the president’s level of interest with study publication dates, they generally follow the same trend of level of interest and number of studies published. This exemplifies the cyclical effect that occurs in the process of conducting scientific research: an area of interest is identified and popularized, thereby increasing funding to that area, which in turn increases the popularity of that area of research, etc. Despite politicians having a very different career field than clinical researchers, they can still have a huge impact on what research is being conducted and when.

The next component to examine is military status of the subjects, seen in Figure 2. Generally, both articles including females and all articles follow the same quantitative trend with regard to status of their subjects. The majority of studies (28 total) identified their subject’s status as a mix, followed by not specified, veterans, active, and service members. The similarities of the quantities, with respect to number of articles in each category, implies that subject military status has minimal effect on participation in combat amputee studies. The fact that the two highest categories were mixed and not specified is indicative of a lack in reported evidence on the researcher’s part for their subject’s military status. This lack of reporting could be due to the fact that military status
has no real biological significance or the assumption that individuals were dismissed due to disability.

Next, amputation types were examined in Figure 3. The results of this study show that the most common amputation type in all articles as a mix (lower and/or upper extremity), followed by lower limb. To contextualize these results, the majority of amputations in the United States are lower limb which account for approximately 65% of amputation types. Another factor to consider is the most common causes of amputation for many combat amputees are explosions and vehicular accidents, which could explain the prevalence of lower limb amputees as subjects in these articles. The impacts of this prevalence could result in less knowledge of upper extremity amputations, and therefore less informed treatment. Even though lower limb amputees are more common in the United States, neglecting upper extremity amputees in research is a disservice to them and their care.

The biological factors and priorities for upper extremity and lower extremity amputations are completely different, especially when considering potential prosthetic use. Upper extremities function in a very different way and at a very different level than lower extremities in day to day life, evident from the distinctions in uses and dexterity. Meaning, in general, people do not walk on their hands and pick things up or type with their feet. However, even at the basic biological level the musculoskeletal systems of upper and lower limbs are only 27% similar, while the skeletal systems are 93% similar. The lack of similarity in musculoskeletal systems was reported to indicate that the way muscles attach to bones are inherently different, especially when comparing the forearm to the leg and the hand to the foot (24). Since upper extremity musculoskeletal systems
are inherently different than that of lower extremities, this could be another reason why there is less research.

Finally, the last two aspects of the results for analysis are article affiliations and overall sex proportions. This study found that the majority of all articles were in some way affiliated with military institutions and only 8 articles (0.1%) had no military affiliations at all. Generally, all articles followed similar trends in terms of quantity of affiliations, however one interesting result was the near equal amount of affiliations to veteran affairs for both only female-inclusive articles and all articles. This could mean that veterans affairs departments have more regulations they are required to follow, they are in contact with more female combat amputees, or other reasons that would explain the equity between sexes in their pooled subject populations.

The fact that the majority of the research is affiliated with the military makes sense, as the subject pool is of combat amputees, however this large affiliation rate could also be impacting the science. For instance, if these military groups are ordered to look into specific areas of research, they have to comply, which could leave other areas of research unexplored. With all science, the areas that are studied in depth are the ones that are of the most interest to scientists and affiliated organizations, thus it is an inevitability that some area of research is ignored.

In order to contextualize these results, the overall proportions of identified sex were determined from the articles analyzed. The results showed 43% of articles were female-inclusive in their subject pool, 38% did not identify the sex of their subjects, and 19% were male-only studies. Considering that all of these studies were published within
20 years, after the NIH policy highlighting the importance of including females and other minority groups in research had gone into effect, the proportion of female-inclusive studies still do not reflect the desired result. Of all the articles, approximately 74% were published in the last 10 years. In those articles, 9 identified race/ethnicity, and 6 identified 2 or more race/ethnicities. In terms of identified sex proportions, approximately 42% did not identify sex of their subjects, 36% were female-inclusive articles, and 23% used only male subjects. From this breakdown, the data appears to show a decrease in female-inclusive articles, and an increase in unidentified and male-only articles for combat amputees.

The biological implication of these findings can seriously impact how female combat amputees are researched and treated medically. For example, articles including female combat amputees have been found to most often use a mix of different amputation types in their studies, however the second most studied amputation population are lower limb amputees. As previously cited from Bruening et al., females have different gait kinesiology from males, specifically in their range of motion. Therefore, if the research on gait kinesiology is primarily male dominated, or sex is not included as a variable, then females are at a disadvantage in care. For instance, if physical therapists and prosthetists use the information gathered from research done on male subjects regarding combat amputations for all of their patients, they would not be providing the best course of treatment for female combat amputees that they treat. This frame of thought can be applied to any of the notable biological factors listed previously: differences in muscle architecture/performance, pain response, immune response, and hormonal impact on aging as well as diseases, etc. These considerations must also apply to neglected
races/ethnicities as well. Essentially, if a population’s specific traits are not taken into consideration when conducting research that could potentially affect them, that population is put at a disadvantage.

To go back to the examination of policy changes within the scientific community and the military and how they affected publications, this analysis could be true for any type of policy change. This study found that the recommendations of inclusive policies in scientific research did not have an effective impact on publications. While it is too soon to determine the impact of these policies becoming codified on publications, the result of the recommendations implies that these policies do not change how research is formatted. In thinking of solutions to fix this issue, the most obvious would be to implement more thorough regulations on the reasoning provided when disregarding sex as a biological variable. For example, if researchers were investigating a disease that only affects males, then this research should continue because of the potential impact it could have on the male population. However, if the background investigations reveal that prior experimentation had only been conducted on a white-male population, then future research should be liable to investigate the potential impacts of the research on a diverse population.

When considering the inclusion of racial/ethnic minorities in particular, the scientific community still debates the necessity of considering race as a biological factor. While the NIH recommended race/ethnicity to be reported since their 1993 policy change, similarly to female subjects, this study found that racial and ethnic minorities are still underrepresented and the impacts of the 2016 codification are still too early to determine. However, a recent report argues that studies reporting race as a biological
variable only further divide people rather than better informing them (104). Rather, these researchers suggest ethnicity or genotypes be specified so that the more applicable analyses can occur because different races have not been shown to have different biological mechanisms. Essentially, these researchers acknowledge that there are social, cultural, economic, and genotypic variations between populations and they argue that these differences be analyzed by their specific affect on study populations rather than grouping these differences under the label of race. However, regardless of how this information is labeled, it should still be collected from subjects because of the social, cultural, economic, and genotypic differences between populations that affect their day to day lives.

In terms of the military policy changes, this study found racial/ethnic minorities and females were still underrepresented. Especially taking into consideration the desegregation of the armed forces happened in 1948 and the prevalence of racial/ethnic minorities that experience amputations. Whereas policy changes regarding females in combat taking effect in 2016 and the smaller portion of female amputees, it is more understandable why the included articles had fewer females within their subject populations.

In order to fix this lack of representation of female and racial/ethnic minorities, multiple factors must be changed. First, the recognition that scientific research and the military is biased towards white male individuals. If further research were conducted accounting for how many articles that included females or racial/ethnic minorities were authored by women or people of those racial/ethnic minorities, for example, it could reinforce this claim of bias. Upon recognizing this bias, further steps can be taken to
ensure equality. Some of these steps could include implementation of requirements, with consequences if unfollowed, that result in equal opportunities across a diverse population.
CONCLUSION

The results of this study support the proposed hypothesis: due to the historical exclusion of females and other minority groups in combat and in clinical research, the collected data does not accurately reflect the diversity of the population in terms of sex, gender, or race. The subqueries regarding race/ethnicity overall identified sex proportions also found that little racial/ethnic inclusion occurs in these articles, and overall female inclusion in published articles seems to be trending down over the past 20 years. Some possible explanations for these results are the smaller quantity of females in the military and the amputee communities, the uncontrollable factor of who receives combat amputations, the lack of necessity for combat amputations due to no recent conflict involvement, and the length of time since the changes to policy have been made. The importance of this research primarily lies in the implications for female combat amputee medical treatment, as well as treatment of females in the military and scientific research communities. While there are many factors that contribute to the lack of female participation in clinical research and the military, one way to improve female participation is to hold communities accountable to the policies put in place. Legally, the changes have been made to policy to ensure females and minorities have equal treatment, although this equality in treatment has not been effectively put into practice with regard to the military and clinical research. One way to hold the scientific community accountable would be to have the NIH require researchers report subject sex and race/ethnicity target ratios with their proposals, if they fit within a certain range the studies could be approved for additional funding and if not they could be denied additional funding. To keep researchers honest, there could be a mandatory demographic
ratio report to the NIH once subjects have been confirmed. Essentially, tactics must be
implemented that will reinforce the inclusive policies if we want to see true change
within research. The same mindset can be applied to the military community. Fair
repercussions for not following the inclusive policies that the military has claimed to
have implemented would enact real change. Improving treatment of females and
minorities in these areas is important for equality as a whole, as well as important for
recognizing that there are many areas to improve in when it comes to historically
marginalized populations.
REFERENCES


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Victoria Eichorn is a student at the University of Maine in the School of Biology and Ecology. She will graduate in May of 2023 with a Bachelor of Science degree in Biology with a concentration in Pre-Medical Studies and a minor in Folklore and Traditional Arts. During her undergraduate education she worked off-campus part time as a Maintenance Technician at Dirigo Pines Retirement Community, and spent a summer as an intern at Hanger Clinic. She was also a member of the University of Maine Women’s Club Soccer, University of Maine Women’s Club Rugby, Partners for World Health, University of Maine Volunteer Ambulance Corps and the University of Maine chapter of Phi Kappa Beta Honors Society. Following graduation, Victoria will be attending the University of Hartford’s Masters of Science Prosthetics and Orthotics graduate program. She is very excited to pursue a career in prosthetics and orthotics which will allow her to continuously learn, work creatively, and help people on a daily basis.