AWARD NUMBER: W81XWH-20-1-0941

TITLE: Epidemiology of Combat Ocular Injury to Guide Prolonged Field Care

PRINCIPAL INVESTIGATOR: Amanda Staudt, MPH, PhD

CONTRACTING ORGANIZATION: The Geneva Foundation at
U.S. Army Institute of Surgical Research (USAISR)
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REPORT DATE: October 2023

TYPE OF REPORT: Annual, Y3

PREPARED FOR: U.S. Army Medical Research and Development Command
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Epidemiology of Combat Ocular Injury to Guide Prolonged Field Care

5a. CONTRACT NUMBER W81XWH-20-1-0941

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Amanda Staudt, MPH, PhD; Jennifer Trevino, MBA

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

U.S. Army Institute of Surgical Research (USAISR)
3698 Chambers Pass, BLDG 3611 JBSA
Fort Sam Houston, 78234

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The key objective of the proposed study is to create an algorithm to inform treatment requirements timeline in a prolonged field care setting to reduce the number of patients with loss of visual acuity. Predicted delays in medical evacuation in future conflicts, will lead to the increased extent of prolonged field care, which could potentially lead to an increase in loss of visual acuity. However, at present, the threshold of allowable maximum time before initiation of primary repair to minimize loss of visual acuity remains unclear. Thus, the identification of the maximum time to treatment in current (shorter) timelines will inform treatment guidelines and expectations during prolonged field care.

In this pursuit, we plan to use a two-part solution to inform new treatment guidelines and expectations during prolonged field care for patients with ocular injury. In the first part, determining the burden of injury for each diagnosis, results will enable prioritization of research initiatives to the ocular injuries determined to cause most disability, which will help identify the most impactful areas in reference to the results from the second part of the project. In the second part, determining the association of time to primary repair with final visual acuity, results will contribute to the development of evidence-based guidelines for care of ocular injuries during prolonged field care.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRDC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**	UU	18	**19b. TELEPHONE NUMBER** *(include area code)*
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1. **INTRODUCTION:**
   The key objective of the proposed study is to create an algorithm to inform treatment requirements timeline in a prolonged field care setting to reduce the number of patients with loss of visual acuity. Predicted delays in medical evacuation in future conflicts, will lead to the increased extent of prolonged field care, which could potentially lead to an increase in loss of visual acuity. However, at present, the threshold of allowable maximum time before initiation of primary repair to minimize loss of visual acuity remains unclear. Thus, the identification of the maximum time to treatment in current (shorter) timelines will inform treatment guidelines and expectations during prolonged field care.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).
   DALYs
   DMDC
   DVEIVR
   TMDS
   Ocular injury
   Transport timing
   Prolonged field care
   Combat

ACCOMPLISHMENTS:

What were the major goals of the project?

The goals of this project are to develop knowledge products to answer the study's specific aims.

The project's Specific Aims are as follows:

Specific Aim 1. Determine the burden of ocular injury for each diagnosis.

Aim 1.1 Establish disability weights for each diagnosis. Global Burden of Disease Study unique health states will be cross walked with patient diagnosis data.

Aim 1.2 Calculate the Disability Adjusted Life Years (DALYs) of ocular injury for each diagnosis. Daly's calculations will determine the years of life lost to disability among all ocular injuries.

Specific Aim 2. Define maximum time from injury to primary repair to reduce loss of visual acuity.

Aim 2.1 Determine the association between times to treatment with loss of final visual acuity. This association will be tested using multivariable logistic regression models stratified by major types of ocular trauma. Covariates will include severity of injury, as measured by the ocular trauma score, and mechanism of injury.

Aim 2.2 Extrapolate the regression model equation to predict odds of loss of visual acuity with time to treatment extended to 24, 48, and 72 hours. For each diagnosis, using the intercept and

regression coefficients calculated in Aim 2.1, the odds of loss of final visual acuity will be calculated using the log (odds) model equation at 24, 48, and 72 hours.

What was accomplished under these goals?

1) **Major Activities: The research team continued to work towards accomplishing the SOW deliverables (below):**

The approved SOW was broken down by specific aims and subtasks. During the previous and current reporting period, we achieved Specific Aim 1, Major Task 1, Subtask 1-5, Major Task 2, Subtasks 1-1b, and Major Task 3, Subtask 1 which are as follows:

Major Task 1

Subtask 1: Hired research staff. Prepared cooperative research and development agreements (CRADAs), MOUs, and MOAs as required. Prepared research protocol and regulatory documents. Research protocols included the following:

- H-20-023 "Epidemiology of Combat Ocular Injury to Guide Prolonged Field Care, and
- H-21-023 "Elicitation of disability weights among combat casualties using a web-based survey".

Completed, 100% of regulatory submissions. However, please note, both protocols will be ongoing through the end of the study (month 48).

Subtask 2: Prepared Defense Health Agency (DHA) Data Sharing Agreement Application (DSA) application to include, Defense and Veterans Eye Injury and Vision Registry (DVEIVR), Theater Medical Data Store (TMDS), and survey approval for both protocols (H-20-023 and H-21-023). Completed, 100% of initial, interim, and annual submissions. However, please note, DHA DSA applications are ongoing following amendments, modifications, and annual renewals.

During this reporting period, the current DSA renewal expired 30 Sep 2023 with grace period of 60-days (30 November 2023). The signed renewal was submitted to the DHA DSA for review.

Subtask 3: Requested identifiable datasets directly from DVEIVR, and access to TMDS in accordance with approved protocol (H-20-023) and DHA DSAA. Completed, 100%.

Subtasks 4 Create Health Insurance Portability and Accountability Act (HIPAA) compliant database. For this deliverable, the research team created the survey in REDCap (Research Electronic Data Capture) for the HIPAA compliant database. The HIPAA compliant database/REDCap is on the Geneva Foundation server at https://redcap.genevausa.org/redcap, and only accessible to the research team. Completed, 100%.

Subtask 5: Identified patients meeting inclusion criteria using the WROTD and DVEIVR. The research team received, cleaned, and identified which patients met inclusion criteria using DVEIVR data following the approved protocol (H-20-023). Completed, 100%.

Milestone Achieved: Research staff hired and trained. All agreements (CRADA, MOU, and MOA), IRB approved protocols, and HRPO second level review and approvals were obtained. Completed, 100%.

Milestone Achieved: DHA DSA application initial approvals, modifications, and renewals were approved. Completed, 100% (pending modifications and/or renewals annually).

Milestone Achieved: Team obtained WROTD, DVEIVR, and TMDS data. All data is maintained in HIPAA compliant database. Completed, 100%.

Major Task 2

Subtask 1: Establish disability weights for each diagnosis. The study team determined the best way to establish disability weights for each diagnosis, which included the protocol H-21-023 that used a web-based survey to establish disability weights.

Using a web-based survey, we are using paired comparison questions of two hypothetical health states, where the participant will select which person, they deem to be healthier. We will use lay definitions for each health state, which were developed by the GBD. In addition, we will also include the following health state:

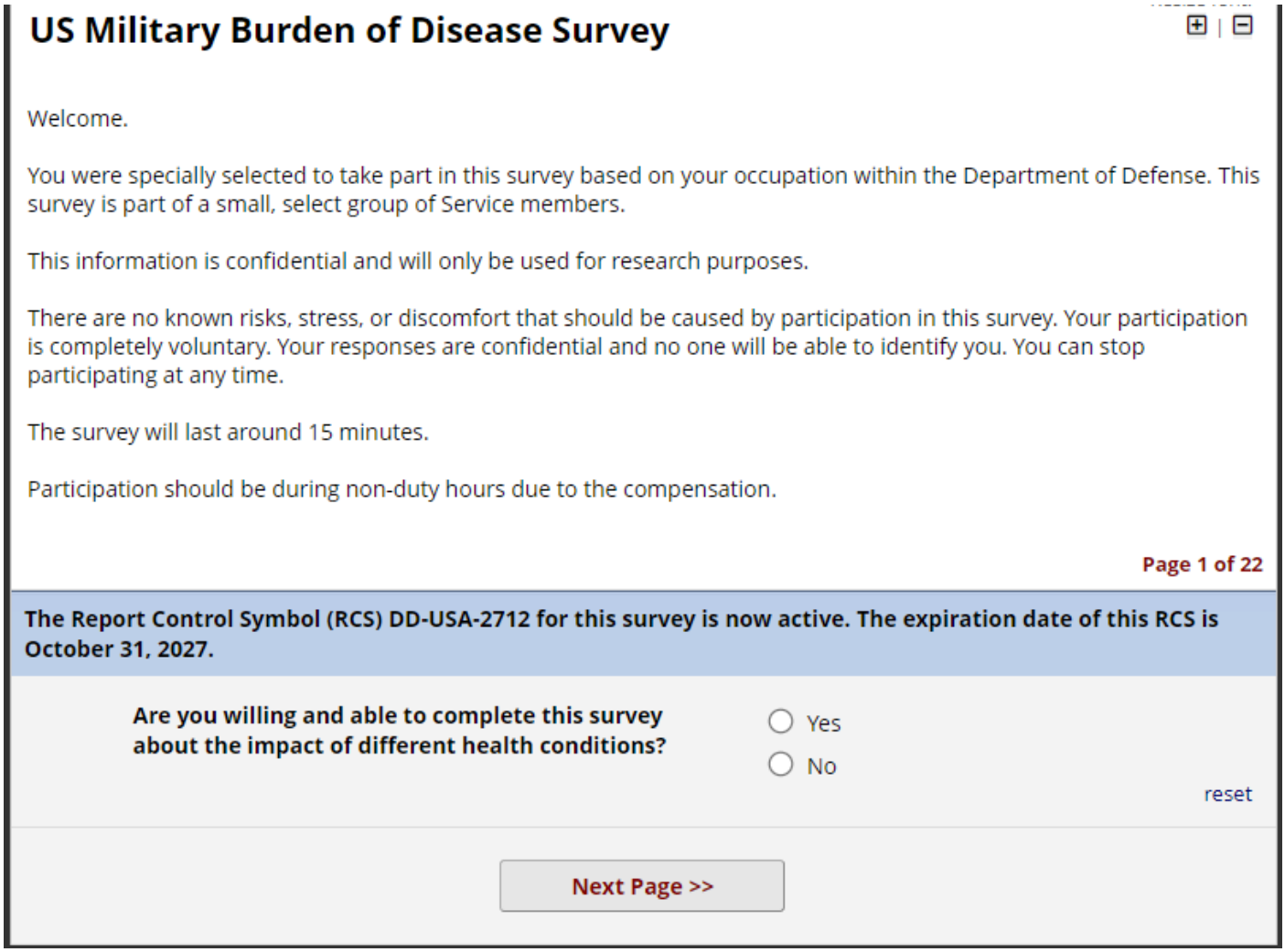
Health state	Lay definition
Photophobia	light causes discomfort and need to close eyes, light may cause headaches

The study team-initiated wave 1 and wave 2 of survey. Upon final data collection and analysis, the study PI will be able to establish the disability weights for each diagnosis. Pending completion.

Subtask 1a: Created a web-based survey The web-based survey was created as part of the protocol submission review and approval process. The research survey “US Military Burden of Disease survey includes 383 records, 68 fields, 1 survey instrument, embedded with survey logic (see below). Completed, 100%.

Subtask 1b: Obtain IRB approval to conduct survey. During the previous reporting periods, we received final protocol approval for H-21-023 and survey approval for Report Control Symbol (RCS) DD-USA-2712, "Elicitation of disability weights among combat casualties using a web-based survey,". The protocol and survey are currently active. The expiration date of this RCS is October 31, 2027.

Please note, the survey is ongoing and can be accessed and completed at: https://redcap.genevausa.org/surveys/?s=H34KHCHELJ (below).



US Military Burden of Disease Survey

Welcome.

You were specially selected to take part in this survey based on your occupation within the Department of Defense. This survey is part of a small, select group of Service members.

This information is confidential and will only be used for research purposes.

There are no known risks, stress, or discomfort that should be caused by participation in this survey. Your participation is completely voluntary. Your responses are confidential and no one will be able to identify you. You can stop participating at any time.

The survey will last around 15 minutes.

Participation should be during non-duty hours due to the compensation.

Page 1 of 22

The Report Control Symbol (RCS) DD-USA-2712 for this survey is now active. The expiration date of this RCS is October 31, 2027.

Are you willing and able to complete this survey about the impact of different health conditions?

- ○ Yes
- ○ No

reset

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Subtask 1c: Identify contact information for survey study population. We provided a list of eligible military occupations to Defense Manpower Data Center (DMDC). Using our list, DMDC identified eligible survey participants. DMDC provided a list of email addresses, phone numbers, and service component for all eligible service members. Even if a service member was no longer in a military occupational specialty involving combat, the service member remained eligible for the survey as they were involved in that type of occupation at one point in their career. DMDC provided contact information for wave 1, n=310 potential participants; and wave 2, n=2200 potential participants.

Wave 2 was calculated based on the actual response and completion rate from wave 1 to achieve the minimum of 4,620 observations.

Subtask 1d: Execute the survey. The survey is web-based, and we are recruiting participants using the following three modes including email, virtual meeting platform (i.e., MS teams meeting), texts and phone calls.

Wave 1, n=310 potential participants (completed 100% all contact methods)

Wave 2, n=2200 potential participants (initiated survey including email method, pending MS teams, texts, and phone calls).

Wave 2 will be ongoing and pending completion through month 40 per the current SOW. Recruitment material, as approved by the protocol, will be sent out as part of recruitment process.

Subtask 1e: Analyze results of the survey. Upon survey completion, all survey results will be analyzed. This deliverable will be ongoing through month 44 per the current SOW. Ongoing, pending completion.

Subtask 2: Calculate the Disability Adjusted Life Years (DALYs) of ocular injury for each diagnosis. Upon survey completion, the study team will complete the DALYs calculations. This deliverable will be ongoing through month 44 per the current SOW. Ongoing, pending completion.

Milestone Achieved: Prepare and present preliminary findings. Preliminary findings were included in the DALYs manuscript recently submitted to Ophthalmology. Anticipate completion no later than month 48 per the current SOW.

Milestones: This analysis will provide a comprehensive representation of the burden of combat ocular injuries as weighted by both frequency and severity of injury. This study would be the first of its kind to provide a representation of the actual number of years of healthy life lost to the ocular injury resulting from combat. Pending final survey responses for wave 2. Anticipate final completion no later than month 48 per the current SOW.

Major task 3

Subtask 1: Determine the association between times to treatment with loss of visual acuity at 30 days. The study team is currently refining the statistical models. Pending completion.

2) Specific objectives: Completed/initiated SOW deliverables (Major Task 1, Subtask 1-5, Major Task 2, Subtask 1 (a-e) and 2, Major Task 3, Subtask 1.

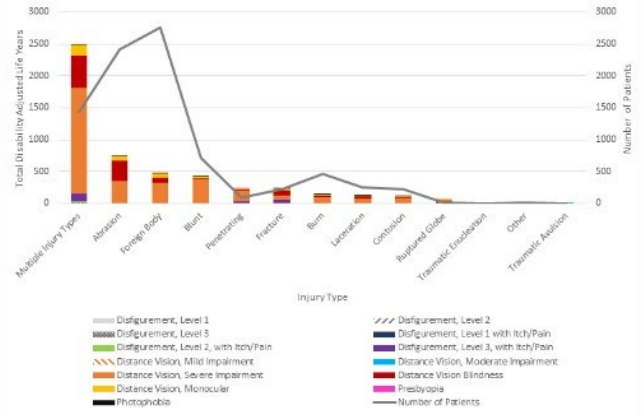
3) Significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative):

- Protocol H-20-023x “Epidemiology of Combat Ocular Injury to Guide Prolonged Field Care” is ongoing and includes 28,554 eye-related patient encounters.
- The manuscript “Disability-Adjusted Life Years due to Ocular Injury Among Combat Casualties, 2001-2020” was submitted to “Ophthalmology” October 2023. Figure 2. Total

disability adjusted life years by injury type, Figure 3. Total disability adjusted life years by age, Figure 4. Total disability adjusted life years by year, and Figure 5. Total disability adjusted life years by injury type percent stratified by health state for male and females, are included below.

- Protocol H-21-023 “Elicitation of disability weights among combat casualties using a web-based survey” is ongoing.
    1. Survey approval and the Report Control Symbol (DD-USA-2712) for "Elicitation of disability weights among combat casualties using a web-based survey” is active with an expiration date of October 31, 2027.
    2. DMDC provided all email addresses for both wave 1 and wave 2 (request # 144017).
    3. The goal of this study is to get approximately 154 participants. This survey study is geared towards the US Military and mimics the global burden of disease study.
        - Wave 1 (n=310) was completed during previous reporting periods.
        - Wave 2 (n=2200) was initiated and included “email method”. The next steps include the following contact methods (Virtual/MS Teams, Text messages, and Phone calls).
        - $2 e-gift card to Amazon were sent out for wave 1 and will be sent out for wave 2. The goal of this strategy is to improve response rate, thereby reducing the potential for non-response error.
- The following five papers are in progress:
    1. Time to treatment of ocular injury among combat casualties, 2001-2020.
    2. Elicitation of disability weights among combat casualties using a web-based survey.
    3. Comparison of disability-adjusted life years using Global Burden of Disease versus US Military Burden of Disease military specific disability weights.
    4. Design to Develop Disability Weights using a Web Based Survey among Combat Casualties: Experience from the US Military Burden of Disease Study” was submitted to Military Medicine (MILMED-S-22-00980-3) was not accepted, but the authors will rework and resubmit.
    5. Traumatic ocular injury among US service members in theater, 2001-2020.

Fig 2A



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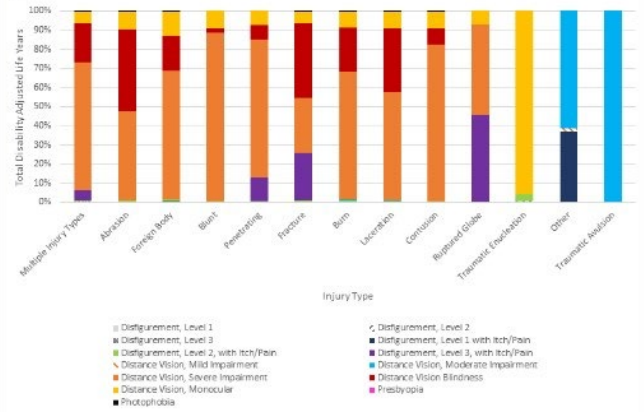
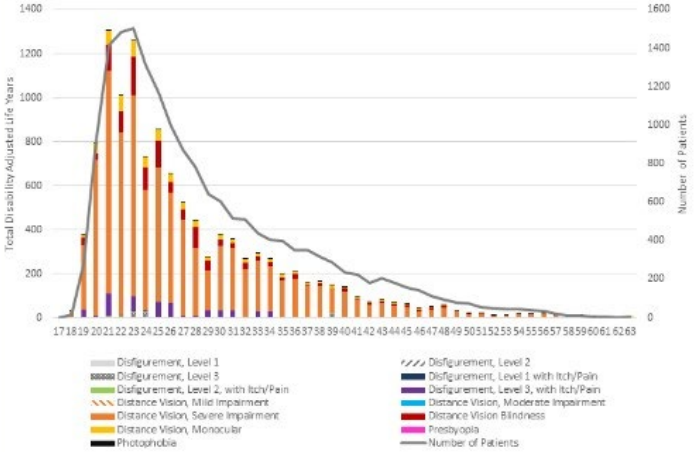


Fig 3A



3B

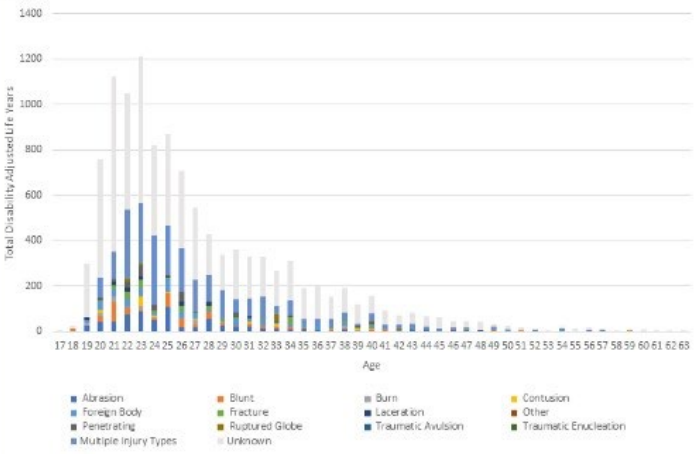
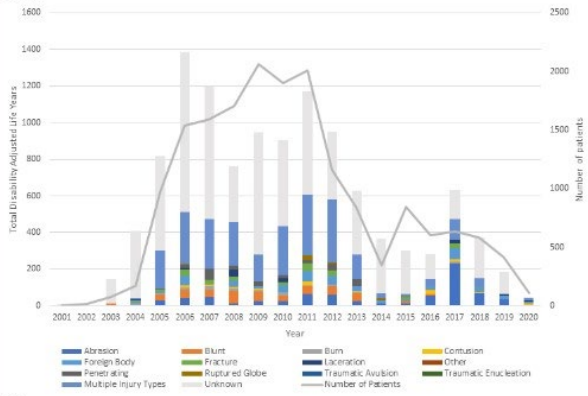


Fig 4A



4B

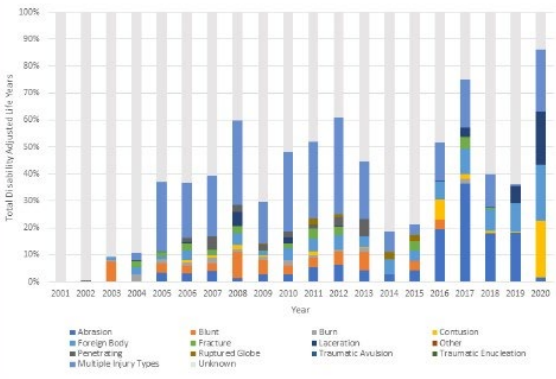
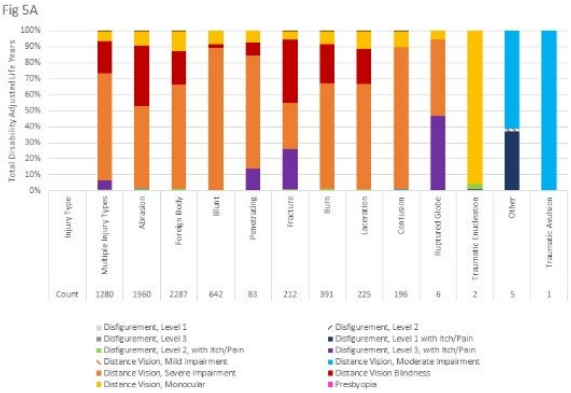
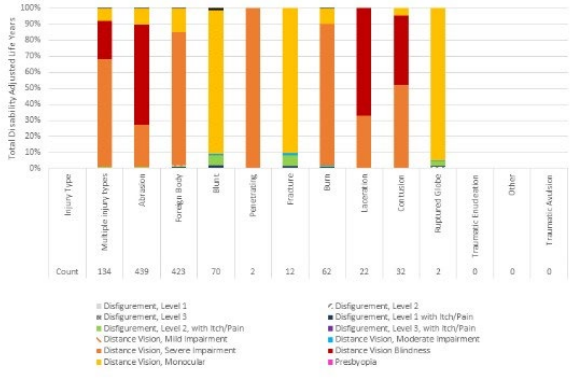


Fig 5A



5B



What opportunities for training and professional development has the project provided?
The research team and subject matter experts continue to meet bi-weekly to collaborate, work towards project deliverables, and cross-train.

Ongoing professional development activities included collaboration with the Global Burden of Disease network. The Global Burden of Disease network is the most prominent developer of disability weights in the world. The PI joined the Global Burden of Disease collaborator network so the team can gain further insight into the disability weight development process.

Additionally, the team conducts a literature review to uncover all publicly available ocular disability weights and learn more about commonly used disability weight development methodology.

How were the results disseminated to communities of interest?
Submitted "Disability-Adjusted Life Years due to Ocular Injury Among Combat Casualties, 2001-2020" manuscript to the scientific journal "Ophthalmology" . These results will be disseminated to the community of interest upon acceptance.

What do you plan to do during the next reporting period to accomplish the goals?
During the next year, the research team will continue working towards accomplishing 100% of the following SOW goals and objectives.

Specific Aim 1. Major Task 2:

Subtask 1: Establish disability weights for each diagnosis. (initiated/ongoing)

Subtask 1d: Execute the survey (i.e., complete all contact methods for wave 2)

Subtask 1e: Analyze results of the survey.

Subtask 2: Calculate the Disability Adjusted Life Years (DALYs) of ocular injury for each diagnosis.

Milestone Achieved: Prepare and present preliminary findings.

Specific Aim 2. Major Task 3:

Subtask 1: Determine the association between times to treatment with loss of visual acuity at 30 days.

Subtask 2: Extrapolate the regression model equation to predict odds of loss of visual acuity with time to treatment extended to 24, 48, and 72 hours.

Milestone Achieved: Using logistic regression, the results will provide guidance for care of ocular injuries during prolonged field care. Working hypothesis: Patients with a longer time from injury to primary repair will have greater effect estimates for loss of visual acuity.

Specific Aim 2. Major Task 4:

Subtask 1: Final report preparation and submission to sponsor including all documents, presentations, and manuscripts.

Milestone Achieved: Publications/Presentations for Specific Aims 1-2.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
A major accomplishment includes the DALYs calculation for ocular injuries among combat casualties. To our knowledge, this is the first quantitative overview of ocular trauma DALYs reported in both the civilian and military literature. Not only do our results identify the impact of ocular injuries on active-duty service members throughout the entire Global War on Terror and lay the groundwork for further research and interventions to mitigate their burden, but the results of this study also indicate that the Global Burden of Disease (GBD) study, a prominent study in health loss quantification, may significantly underrepresent the impact of ocular trauma in global DALYs calculations. If the impact of ocular trauma was represented correctly, we would expect an indirect impact of our study would include improvements to ocular trauma health systems.

What was the impact on other disciplines?
Nothing to Report.

What was the impact on technology transfer?
Nothing to Report.

What was the impact on society beyond science and technology?
Nothing to Report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change
A no cost extension was approved by the sponsor and the SOW was updated to reflect the additional 12-months.

Actual or anticipated problems or delays and actions or plans to resolve them
A no cost extension was approved. The new project end date is 30 September 2024.

Changes that had a significant impact on expenditures
No change.

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

Significant changes in use or care of human subjects
NA

Significant changes in use or care of vertebrate animals
NA

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

6. PRODUCTS:

Publications, conference papers, and presentations
Completed and submitted OPHTHA-S-23-02561 "Disability-Adjusted Life Years due to Ocular Injury Among Combat Casualties, 2001-2020" to Ophthalmology on 05 October 2023.

Journal publications.
The following five papers are in progress:

1. Time to treatment of ocular injury among combat casualties, 2001-2020.
2. Comparison of disability-adjusted life years using Global Burden of Disease versus US Military Burden of Disease military specific disability weights, and Disability-Adjusted Life Years due to Ocular Injury Among Combat Casualties, 2001-2020.
3. Elicitation of disability weights among combat casualties using a web-based survey.
4. Design to Develop Disability Weights using a Web Based Survey among Combat Casualties: Experience from the US Military Burden of Disease Study" was submitted to Military Medicine (MILMED-S-22-00980-3) was not accepted, but the authors will rework and resubmit.
5. Traumatic ocular injury among US service members in theater, 2001-2020

Books or other non-periodical, one-time publications. Nothing to Report.

Other publications, conference papers and presentations. Nothing to Report.

Website(s) or other Internet site(s)
The Geneva Foundation highlighted the Eye Epi grant and grant PI (Dr. Amanda Staudt) as a "Researcher to watch". Platforms included twitter and LinkedIn:
https://genevausa.org/news/story/epidemiology-of-combat-ocular-injury/

https://redcap.genevausa.org/redcap (internal web-based HIPAA Compliant Database)

https://redcap.genevausa.org/surveys/?s=H34KHCHELJ (external web-based survey link)

Technologies or techniques
Nothing to Report.

Inventions, patent applications, and/or licenses
Nothing to Report.

Other Products
Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Amanda Staudt, PhD, MPH
Project Role:	Geneva/USAISR Principal Investigator (PI)/Epidemiologist
Nearest person month worked:	2.2
Contribution to Project:	Dr. Staudt has performed work in the area of regulatory compliance and submissions, and data access, data analysis, and manuscript writing.
Funding Support:	Geneva Foundation (W81XWH-20-1-0941)

Name:	Jennifer Trevino, MBA
Project Role:	Geneva/USAISR Program Manager/Co-Investigator
Nearest person month worked:	1.2
Contribution to Project:	Ms. Trevino has performed work in the area of regulatory compliance and submissions, program/project management, and data access, and manuscript writing.
Funding Support:	Geneva Foundation (W81XWH-20-1-0941)

Name:	LTC Marcus Colyer, MD
Project Role:	USUHS Site PI
Nearest person month worked:	3
Contribution to Project:	LTC Colyer has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma and critical review of manuscripts.
Funding Support:	US Army

Name:	CPT Grant Justin
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	CPT Justin has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma and critical review of manuscripts.
Funding Support:	US Army

Name:	Juanita Haasma, PhD
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	Dr. Haagsma has performed work in the area of providing SME support in the area of burden of disease and critical review of manuscripts.
Funding Support:	NA

Name:	William Gensheimer
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	Mr. Gensheimer has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma and critical review of manuscripts.
Funding Support:	US Army

Name:	MAJ Karina Bostwick
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	MAJ Bostwick has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma.
Funding Support:	US Air Force

Name:	Boonkit Purt
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	Boonkit Purt has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma.
Funding Support:	US Army

Name:	Nathan Davidson
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	Nathan Davidson has provided SME support in the area of Ophthalmology and ocular trauma.
Funding Support:	US Army

Name:	Akash Halagur
Project Role:	Collaborator/ MD Candidate
Nearest person month worked:	3
Contribution to Project:	Akash Halagur has provided SME support in the area of Ophthalmology and ocular trauma and manuscript writing.
Funding Support:	NA

Name:	Mark Travor
Project Role:	Collaborator
Nearest person month worked:	3
Contribution to Project:	Mark Travor has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma, data mapping, and manuscript writing.
Funding Support:	NA

Name:	Emily Levine
Project Role:	Collaborator
Nearest person month worked:	3
Contribution to Project:	Emily Levine has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma, data mapping, and manuscript writing.
Funding Support:	NA

Name:	Andrew Catomeris
Project Role:	Collaborator
Nearest person month worked:	3
Contribution to Project:	Andrew Catomeris has performed work in the area of providing SME support in the area of Ophthalmology and ocular trauma and data mapping.
Funding Support:	NA

Name:	Frances Silva
Project Role:	Collaborator
Nearest person month worked:	1

Contribution to Project:	Frances Silva has performed work in the area of providing SME support in the area of Ophthalmology.
Funding Support:	NA

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Nothing to Report.

What other organizations were involved as partners?
Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: Attached

9. APPENDICES:

OPHTHA-S-23-02561 “Disability-Adjusted Life Years due to Ocular Injury Among Combat Casualties, 2001-2020” PDF