



Agent Orange & Risk of Pancreatic Carcinogenesis

**Proposal Prepared for Donald Pugh
September 2022**

Stanford Project Team

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Summary

We aim to study the incidence of pancreatic cancer in veterans with and without exposure to Agent Orange (AO) and/or 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD) in a national historic cohort controlling for confounding factors to improve specific knowledge on this epidemiological question. In addition, we expect to evaluate the effect of chemoprevention on the risk and incidence of pancreatic cancer in this population. Our findings may improve understanding of environmental risk factors and pancreatic cancer. In addition, we plan to build on evidence in the growing field of chemoprevention for pancreatic cancer.

Background

Up to 4.3 million Americans served in the Vietnam War and were potentially exposed to chemical defoliants commonly known as Agent Orange (AO) and other chemicals. This exposure has been linked to several cancers including sarcoma, non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and Hodgkin's lymphoma. There is additional, limited evidence that indicates carcinogenesis in laryngeal, lung, prostate, and bladder cancer. However, there is insufficient evidence to conclude that the same exposure is linked to pancreatic cancer. While several studies have shown increased incidence in nurse veterans serving in Vietnam, inadequately powered studies and lack of ability to collect and control for confounding variables have led to conflicting results in male Vietnam veterans across multiple countries. This conflicting data for American veterans requires a carefully designed and powered study to evaluate the risk of pancreatic cancer.

Clinical Impact / Expected Outcome

Based on our study design we expect to conduct a review of the largest number of pancreatic cancer cases studied for an association with AO exposure in an American veteran population. Current research is limited to less than 100 cases of pancreatic cancer in this population. Globally, including veterans from other countries, the largest study to date is approximately 500 cases.

This study may allow us to have higher statistical power in detecting an association of AO exposure on the risk of pancreatic cancer which has had conflicting results in literature. In addition, we hope to control for confounding factors which may increase or decrease risk of pancreatic cancer. Some of these findings may be valuable in providing support for risk reduction strategies in the future. The findings could be relevant to the veteran population and may provide rationale for study in broader populations.

Research Plan

We expect to study up to 700 cases of eligible pancreatic cancer in veterans born after January 1, 1935 and match to a demographically similar cohort without pancreatic cancer. The main exposure we are examining will be AO/TCDD. This study will be designed as retrospective analysis and all data will be housed on internal VA data management per requirements. Data will be analyzed retrospectively with univariate analysis and multivariate analysis. Secondary analysis may include survival analysis of pancreatic cancer. This project is estimated to reach completion at 12 months after approval and data access.

Gift Opportunity

The anticipated cost of this project is \$25,000 and includes expected costs for part-time support of a postdoctoral researcher, analysis, access to data and administrative costs related to executing the project.

The gift opportunity in this proposal provides a description of current and anticipated expenses. As the project progresses, aspects of staff and budget may change. If the project is discontinued while any funds remain, the remaining funds will be used at the direction of Dr. George Poultsides for pancreatic cancer research. These gift funds will be subject to Stanford University's infrastructure charge (currently 8%), which helps to defray the related, but indirect, costs associated with the activities supported by the gift; this was considered in determining the budget/costs of the project.