

## Brief Report

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# Agent Orange Exposure and Dementia Diagnosis in US Veterans of the Vietnam Era

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## Key Points

**Question** Is Agent Orange exposure associated with an increased risk of dementia diagnosis in US veterans of the Vietnam era?

**Findings** In this study of more than 300 000 veterans, those with Agent Orange exposure in their medical records were nearly twice as likely as those without exposure to receive a dementia diagnosis, even after adjusting for medical and psychiatric comorbidities and other variables.

**Meaning** Per this analysis, Agent Orange exposure may increase risk of dementia.

## Abstract

**Importance** Agent Orange is a powerful herbicide that contains dioxin and was used during the Vietnam War. Although prior studies have found that Agent Orange exposure is associated with increased risk of a wide range of conditions, including neurologic disorders (eg, Parkinson disease), metabolic disorders (eg, type 2 diabetes), and systemic amyloidosis, the association between Agent Orange and dementia remains unclear.

**Objective** To examine the association between Agent Orange exposure and incident dementia diagnosis in US veterans of the Vietnam era.

**Design, Setting, and Participants** This cohort study included Veterans Health Administration data from October 1, 2001, and September 30, 2015, with up to 14 years of follow-up. Analyses were performed from July 2018 to October 2020. A 2% random sample of US veterans of the Vietnam era who received inpatient or outpatient Veterans Health Administration care, excluding those with dementia at baseline, those without follow-up visits, and those with unclear Agent Orange exposure status.

**Exposures** Presumed Agent Orange exposure documented in electronic health record.

**Main Outcomes and Measures** Fine-Gray competing risk models were used to compare the time to dementia diagnosis (with age as the time scale) for veterans with vs without presumed Agent Orange exposure (as per medical records), adjusting for demographic variables and medical and psychiatric comorbidities.

**Results** The total sample was 511, 189 individuals; after exclusions, 316 351 were included in analyses. Veterans were mostly male (n = 309 889 [98.0%]) and had a mean (SD) age of 62 (6.6) years; 38 121 (12.1%) had presumed Agent Orange exposure. Prevalence of most conditions, including Parkinson disease, diabetes, and amyloidosis, was similar at baseline among veterans with and without Agent Orange exposure. After adjusting for demographic variables and comorbidities, veterans exposed to Agent Orange were nearly twice as likely as those not exposed to receive a dementia diagnosis over a mean (SD) of 5.5 (3.8) years of follow-up (1918 of 38 121 [5.0%] vs 6886 of 278 230 [2.5%]; adjusted hazard ratio: 1.68 [95% CI, 1.59-1.77]). Veterans with Agent Orange exposure developed dementia at a mean of 1.25 years earlier (at a mean [SD] age of 67.5 [7.0] vs 68.8 [8.0] years).

**Conclusions and Relevance** Veterans with Agent Orange exposure were nearly twice as likely to be diagnosed with dementia, even after adjusting for the competing risk of death, demographic variables, and medical and psychiatric comorbidities. Additional studies are needed to examine potential mechanisms underlying the association between Agent Orange exposure and dementia.

<https://jamanetwork.com/journals/jamaneurology/article-abstract/2774857>