



Airborne Hazards and Burn Pits Research Compilation

Airborne Hazards and Burn Pits Center of Excellence

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- Background** The Airborne Hazards and Burn Pits Center of Excellence (AHBPCE), located at the New Jersey War Related Illness and Injury Study Center (NJ WRIISC), was established as a VA Center of Excellence in 2019 and specializes in clinical and translational research. Scientific insights are used to help improve health outcomes for Veterans exposed to airborne hazards while deployed.
- Objective** AHBPCE advocates for Veterans who have concerns about potential adverse health outcomes related to airborne hazard exposures. Through ongoing research and clinical work, the AHBPCE seeks to understand and find solutions for these exposure-related health issues.
- Approach** AHBPCE researchers and collaborators conduct investigator-initiated pre-clinical, clinical and epidemiological research. These efforts extend to use of large databases, such as the Airborne Hazards and Open Burn Pit Registry (AHOBPR), to identify a range of health concerns related to airborne hazard exposure, including respiratory concerns, unexplained shortness of breath and other health issues among Veterans and active-duty servicemembers.
- Value** AHBPCE responds to the growing need for deeper knowledge of respiratory health concerns related to airborne hazards and open burn pits among Veterans and active-duty servicemembers.
- Collaboration** To expand AHBPCE's reach and goals, partnerships and collaborations are widespread across research universities, VA agencies and many other experts across the country. These partnerships allow the Center to pursue more in-depth research questions and explore new ways to understand and treat Veterans who have been exposed to airborne hazards.
- Contacts** The co-directors of AHBPCE are Dr. Anays Sotolongo and Dr. Michael Falvo. The primary performing site for these efforts is the New Jersey War Related Illness and Injury Study Center (NJ WRIISC) in East Orange, NJ. The study team welcomes collaborations and can be contacted by email at VHAEASAirHazardsCoE@va.gov.

Aslaner, D. M., Saldaña, T. A., MacKenzie, D. M., O'Piela, D. R., Miller, R. A., Schwieterman, N. A., Falvo, M. J., Gorr, M. W., & Wold, L. E. (2022). **Short-term PM exposure and social stress cause pulmonary and cardiac dysfunction.** *Toxicology letters*, 370, 66–73. <https://doi.org/10.1016/j.toxlet.2022.09.006>

This data indicates that short-term exposure to PM_{2.5} with or without stress causes a clear reduction in pulmonary and cardiac function. This model is well-suited for the study of military and other occupational exposures, and future work will identify potential mechanisms, including the inflammatory progression of these co-exposures.

Davis, C. W., Lopez, C. L., Bell, A. J., Miller, R. F., Rabin, A. S., Murray, S., Falvo, M. J., Han, M. K., Galban, C. J., & Osterholzer, J. J. (2022). **The Severity of Functional Small Airway Disease in Military Personnel with Constrictive Bronchiolitis as Measured by Quantitative Computed Tomography.** *American journal of respiratory and critical care medicine*, 206(6), 786–789. <https://doi.org/10.1164/rccm.202201-0153LE>

In this study, we sought to determine whether a non-invasive imaging biomarker of small airway disease (fSAD) is increased in military personnel constrictive bronchiolitis relative to healthy subjects as well as those with varying severity of COPD.

Therkorn, J. H., Qian, W., Toto, D. R., & Falvo, M. J. (2022). **An analysis of alternative forced oscillation technique reporting and validation methods for within- and between-sessions in healthy adults.** *Scientific reports*, 12(1), 13119. <https://doi.org/10.1038/s41598-022-17264-2>

Our analyses support current ERS reporting recommendations for healthy adults. Future work should apply this analytic approach to patient populations.

Therkorn, J. H., Hu, S., Sotolongo, A. M., Christie, I. C., Wu, T. D., Van Doren, W. W., Sajja, V., Jani, N., Klein-Adams, J. C., Helmer, D. A., & Falvo, M. J. (2022). **Relationship between clinician documented blast exposure and pulmonary function: a retrospective chart review from a national specialty clinic.** *Respiratory research*, 23(1), 153. <https://doi.org/10.1186/s12931-022-02071-0>

In this referred sample of deployed Veterans, PFT measures of flow, volume, diffusion, and respiratory mechanics were not associated with clinician documented blast exposure per the retrospective chart abstraction methodology applied. Yet, these clinical findings suggest future research should determine and assess distinction between Veteran recollections of perceived blast experiences versus overpressure wave exposure to the respiratory system.

Ibraheem, D. L., Samy, B., Therkorn, J. H., & Falvo, M. J. (2022). **Beyond the Expiratory Limb: A Complete Raw Spirometry Dataset.** *Frontiers in physiology*, 13, 898831. <https://doi.org/10.3389/fphys.2022.898831>

Publicly available spirometry datasets are presently limited to expiratory data only [e.g., National Health and Nutrition Examination Survey ((Centers for Disease Control and Prevention (CDC))]; therefore, the present dataset may foster additional research directed at the inspiratory portion of forced vital capacity maneuvers as well as encourage manufacturer's to consider providing additional variables specific to the inspiratory portion of spirometry.

Rabin, A. S., Davis, C. W., Sotolongo, A. M., Falvo, M. J., & Osterholzer, J. J. (2022). **A Burning Question**. *The New England journal of medicine*, 386(14), 1352–1357. <https://doi.org/10.1056/NEJMcp2119930>

A case study; a 35-year-old man presented to a Veterans Affairs pulmonary clinic with exertional dyspnea and cough. The patient's symptoms began 4 years before presentation and had progressed over time.

Qian, W., Desai, A., Therkorn, J. H., Klein-Adams, J. C., Sotolongo, A. M., & Falvo, M. J. (2022). **Employing the Forced Oscillation Technique for the Assessment of Respiratory Mechanics in Adults**. *Journal of visualized experiments: JoVE*, (180), 10.3791/63165. <https://doi.org/10.3791/63165>

This effort is intended to standardize the use and interpretation of FOT, provide practical suggestions, as well as highlight future questions that need to be addressed.

Qian, W., Klein-Adams, J. C., Ndirangu, D. S., Chen, Y., Falvo, M. J., & Condon, M. R. (2021). **Hemorheological responses to an acute bout of maximal exercise in Veterans with Gulf War Illness**. *Life sciences*, 280, 119714. <https://doi.org/10.1016/j.lfs.2021.119714>

Veterans with GWI had more deformable RBCs in comparison to controls that was unaffected by maximal exercise. Future studies to confirm our findings and identify associated mechanisms are warranted.

Therkorn, J. H., Toto, D. R., & Falvo, M. J. (2021). **A comparison of alternative selection methods for reporting spirometric parameters in healthy adults**. *Scientific reports*, 11(1), 14945. <https://doi.org/10.1038/s41598-021-94120-9>

We recommend future studies be explicit in their description of spirometry acquisition and analysis to facilitate comparability with the published literature.

Falvo, M. J., Sotolongo, A. M., Osinubi, O. Y., Helmer, D. A., Galvin, J. R., & Franks, T. J. (2020). **Diagnostic Workup of Constrictive Bronchiolitis in the Military Veteran**. *Military medicine*, 185(11-12), 472–475. <https://doi.org/10.1093/milmed/usaa192>

As evidenced by this case, arriving at a diagnosis of CB can be challenging as deviation from normal is often subtle and nonspecific. We are working to identify and review self-reported cases of CB in the Airborne Hazards and Open Burn Pits Registry, as well as educate VA and community providers on best practices. We remain committed in addressing service member and veteran concerns and providing the highest quality care they deserve.

Barhorst, E. E., Andrae, W. E., Rayne, T. J., Falvo, M. J., Cook, D. B., & Lindheimer, J. B. (2020). **Elevated Perceived Exertion in People with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Fibromyalgia: A Meta-analysis**. *Medicine and science in sports and exercise*, 52(12), 2615–2627. <https://doi.org/10.1249/MSS.0000000000002421>

People with ME/CFS and FM perceive aerobic exercise as more effortful than healthy adults, but the exact causes are unclear. The large magnitude of this effect merits further exploration of underlying mechanisms that could provide insight into the pathophysiology of ME/CFS and FM or the broader debate about the nature of central and/or peripheral signals that influence RPE.

Lindheimer, J. B., Alexander, T., Qian, W., Klein-Adams, J. C., Lange, G., H Natelson, B., Cook, D. B., Hill, H. Z., & Falvo, M. J. (2020). **An analysis of 2-day cardiopulmonary exercise testing to assess unexplained fatigue.** *Physiological reports*, 8(17), e14564. <https://doi.org/10.14814/phy2.14564>

The methods and findings reported in this article provide a framework for evaluating 2-day CPET reliability and reinforce the importance of carefully considering measurement error in the population of interest when interpreting findings.

Klein-Adams, J. C., Sotolongo, A. M., Serrador, J. M., Ndirangu, D. S., & Falvo, M. J. (2020). **Exercise-Induced Bronchoconstriction in Iraq and Afghanistan Veterans With Deployment-Related Exposures.** *Military medicine*, 185(3-4), e389–e396. <https://doi.org/10.1093/milmed/usz410>

Approximately 17% of our sample of non-treatment seeking deployed Iraq and Afghanistan veterans demonstrated EIB, similar to the general population prevalence. However, persistent respiratory symptoms and alternative indices of probable EIB supports continued monitoring of this population.

Lindheimer, J. B., Stegner, A. J., Wylie, G. R., Klein-Adams, J. C., Almassi, N. E., Ninneman, J. V., Van Riper, S. M., Dougherty, R. J., Falvo, M. J., & Cook, D. B. (2020). **Post-exertional malaise in veterans with gulf war illness.** *International journal of psychophysiology: official journal of the International Organization of Psychophysiology*, 147, 202–212. <https://doi.org/10.1016/j.ijpsycho.2019.11.008>

Not all GV's with GWI experience PEM 24 hours after exercise, and more research is needed to determine the extent that exercise worsens symptoms in GWI.

Lindheimer, J. B., Stegner, A. J., Ellingson-Sayen, L. D., Van Riper, S. M., Dougherty, R. J., Falvo, M. J., & Cook, D. B. (2019). **Influence of pain anticipation on brain activity and pain perception in Gulf War Veterans with chronic musculoskeletal pain.** *Psychophysiology*, 56(12), e13452. <https://doi.org/10.1111/psyp.13452>

Brain responses to nonpainful thermal stimuli in Veterans with CMP are sensitive to pain anticipation, and we recommend accounting for the influence of pain anticipation in future investigations of central nervous system dysfunction in CMP.

Lindheimer, J. B., Cook, D. B., Klein-Adams, J. C., Qian, W., Hill, H. Z., Lange, G., Ndirangu, D. S., Wylie, G. R., & Falvo, M. J. (2019). **Veterans with Gulf War Illness exhibit distinct respiratory patterns during maximal cardiopulmonary exercise.** *PloS one*, 14(11), e0224833. <https://doi.org/10.1371/journal.pone.0224833>

In our sample, veterans with Gulf War Illness adopt a unique exercise ventilatory pattern characterized by reduced respiratory frequency, despite similar ventilation relative to controls. Although the mechanism(s) by which this pattern is achieved remains unresolved, our findings suggest that the components of ventilation should be considered when evaluating clinical conditions with unexplained exertional symptoms.

Garshick, E., Abraham, J. H., Baird, C. P., Ciminera, P., Downey, G. P., Falvo, M. J., Hart, J. E., Jackson, D. A., Jerrett, M., Kuschner, W., Helmer, D. A., Jones, K. D., Krefft, S. D., Mallon, T., Miller, R. F., Morris, M. J., Proctor, S. P., Redlich, C. A., Rose, C. S., Rull, R. P., ... Blanc, P. D. (2019). **Respiratory Health after Military Service in Southwest Asia and Afghanistan. An Official American Thoracic Society Workshop Report.** *Annals of the American Thoracic Society*, 16(8), e1–e16. <https://doi.org/10.1513/AnnalsATS.201904-344WS>

A workshop conducted at the 2018 American Thoracic Society International Conference had the goals of: 1) identifying key studies assessing post-deployment respiratory health, 2) describing emerging research, and 3) highlighting knowledge gaps. The workshop concluded that the relationship of airway disease, including constrictive bronchiolitis, to exposures experienced during deployment remains to be better defined. Future clinical and epidemiologic research efforts should address better characterization of deployment exposures; carry out longitudinal assessment of potentially related adverse health conditions, including lung function and other physiologic changes; and use rigorous histologic, exposure, and clinical characterization of patients with respiratory tract abnormalities.

Butzko, R. P., Sotolongo, A. M., Helmer, D. A., Klein-Adams, J. C., Osinubi, O. Y., Berman, A. R., Ortiz-Pacheco, R., & Falvo, M. J. (2019). **Forced oscillation technique in veterans with preserved spirometry and chronic respiratory symptoms.** *Respiratory physiology & neurobiology*, 260, 8–16. <https://doi.org/10.1016/j.resp.2018.11.012>

In our referral sample, distal airway dysfunction in the presence of preserved spirometry appears common and may represent an at-risk group requiring closer surveillance.

Tanwar, V., Adelstein, J. M., Grimmer, J. A., Youtz, D. J., Katapadi, A., Sugar, B. P., Falvo, M. J., Baer, L. A., Stanford, K. I., & Wold, L. E. (2018). **Preconception Exposure to Fine Particulate Matter Leads to Cardiac Dysfunction in Adult Male Offspring.** *Journal of the American Heart Association*, 7(24), e010797. <https://doi.org/10.1161/JAHA.118.010797>

Conclusions Preconception exposure to PM 2.5 results in global cardiac dysfunction in adult offspring, suggesting that abnormalities during development are not limited to the prenatal or postnatal periods but can also be determined before conception.

Salcedo, P. A., Lindheimer, J. B., Klein-Adams, J. C., Sotolongo, A. M., & Falvo, M. J. (2018). **Effects of Exercise Training on Pulmonary Function in Adults With Chronic Lung Disease: A Meta-Analysis of Randomized Controlled Trials.** *Archives of physical medicine and rehabilitation*, 99(12), 2561–2569.e7. <https://doi.org/10.1016/j.apmr.2018.03.014>

Contrary to prior assumptions, whole-body exercise training is effective for improving pulmonary function in adults with chronic lung disease, particularly spirometric indices. Subsequent studies are necessary to determine the optimal exercise training characteristics to maximize functional improvement.

Falvo, M. J., Lindheimer, J. B., & Serrador, J. M. (2018). **Dynamic cerebral autoregulation is impaired in Veterans with Gulf War Illness: A case-control study.** *PloS one*, 13(10), e0205393. <https://doi.org/10.1371/journal.pone.0205393>

In our sample of Veterans with GWI, dynamic autoregulation was impaired and consistent with greater cerebral hypoperfusion when standing. This reduced CBF may contribute to cognitive difficulties in these Veterans when upright.

Gratz, D., Hund, T. J., Falvo, M. J., & Wold, L. E. (2018). **Reverse Translation: Using Computational Modeling to Enhance Translational Research.** *Circulation research*, 122(11), 1496–1498. <https://doi.org/10.1161/CIRCRESAHA.118.313003>

Animal models provide powerful tools for examining human disease; however, translation of findings from these models to human patients is often challenging. To this end, we discuss modern tools to support the process of selecting and validating animal models with relevance to humans. We draw from data mining and computational modeling approaches to examine how large datasets may be leveraged to identify suitable models with the greatest translational potential.

Slatore, C. G., Falvo, M. J., Nugent, S., & Carlson, K. (2018). **Afghanistan and Iraq War Veterans: Mental Health Diagnoses are Associated with Respiratory Disease Diagnoses.** *Military medicine*, 183(5-6), e249–e257. <https://doi.org/10.1093/milmed/usx108>

Many Afghanistan and Iraq War veterans are diagnosed with both respiratory and mental illnesses. Comprehensive plans that include care coordination with mental health professionals and treatments for mental illnesses may be important for many veterans with respiratory diseases.

Falvo, M. J., Helmer, D. A., Klein, J. C., Osinubi, O. Y., Ndirangu, D., Patrick-DeLuca, L. A., & Sotolongo, A. M. (2018). **Isolated diffusing capacity reduction is a common clinical presentation in deployed Iraq and Afghanistan veterans with deployment-related environmental exposures.** *The clinical respiratory journal*, 12(2), 795–798. <https://doi.org/10.1111/crj.12552>

More than 75% of our sample had normal lung volumes and spirometry on pulmonary function testing; however, an isolated reduction in lung diffusing capacity (DLCO) was observed in 30% of our sample of post-9/11 veterans. An isolated reduction in DLCO is a rare pattern in primary-care seeking dyspneic patients but is commonly associated with underlying pulmonary disease. Post-9/11 veterans with respiratory complaints and an isolated reduction in DLCO should undergo further evaluation.

Falvo, M. J., Chen, Y., Klein, J. C., Ndirangu, D., & Condon, M. R. (2018). **Abnormal rheological properties of red blood cells as a potential marker of Gulf War Illness: A preliminary study.** *Clinical hemorheology and microcirculation*, 68(4), 361–370. <https://doi.org/10.3233/CH-170262>

In this preliminary study, we observed increased deformability along with increased MCH, MCHC and RDW in veterans with GWI+, which may contribute to the symptomatology of GWI. Further research is required to confirm our findings and the role of RBC microrheology in GWI.

Jani, N., Falvo, M. J., Sotolongo, A., Osinubi, O. Y., Tseng, C. L., Rowneki, M., Montopoli, M., Morley, S. W., Mitchell, V., & Helmer, D. A. (2017). **Blast Injury and Cardiopulmonary Symptoms in U.S. Veterans: Analysis of a National Registry.** *Annals of internal medicine*, 167(10), 753–755. <https://doi.org/10.7326/M17-0711>

Using data from the national Airborne Hazards and Open Burn Pit Registry (AHOBPR), we found that that self-reported blast exposure from an improvised explosive device was independently associated with respiratory symptoms among AHOBPR participants.

Chen, Y., Meyer, J. N., Hill, H. Z., Lange, G., Condon, M. R., Klein, J. C., Ndirangu, D., & Falvo, M. J. (2017). **Role of mitochondrial DNA damage and dysfunction in veterans with Gulf War Illness.** *PloS one*, 12(9), e0184832. <https://doi.org/10.1371/journal.pone.0184832>

Veterans with GWI exhibit greater mtDNA damage which is consistent with mitochondrial dysfunction.

Gorr, M. W., Falvo, M. J., & Wold, L. E. (2017). **Air Pollution and Other Environmental Modulators of Cardiac Function.** *Comprehensive Physiology*, 7(4), 1479–1495. <https://doi.org/10.1002/cphy.c170017>

In this comprehensive review, we detail the background and epidemiology of the effects of air pollution and other environmental modulators on the heart, including both short- and long-term consequences. Then, we provide the experimental data and current hypotheses of how pollution is able to cause the CVD, and how exposure to pollutants is exacerbated in sensitive states.

Chen, Y., Hill, H. Z., Lange, G., & Falvo, M. J. (2017). **Salivary Mitochondrial DNA Copy Number Is Associated With Exercise Ventilatory Efficiency.** *Journal of strength and conditioning research*, 31(7), 2000–2004. <https://doi.org/10.1519/JSC.0000000000001932>

Our findings suggest that salivary mtDNAcn is associated with ventilatory efficiency, which may reflect enhanced exercise efficiency as a consequence of greater total mitochondrial content. As saliva collection is noninvasive, stable at room temperature, and less costly in comparison to skeletal muscle and blood, future studies may consider using saliva for the evaluation of mitochondrial content for the purposes of monitoring exercise training as well as optimizing exercise prescription.

Liu, J., Lezama, N., Gasper, J., Kawata, J., Morley, S., Helmer, D., & Ciminera, P. (2016). **Burn Pit Emissions Exposure and Respiratory and Cardiovascular Conditions Among Airborne Hazards and Open Burn Pit Registry Participants.** *Journal of occupational and environmental medicine*, 58(7), e249–e255. <https://doi.org/10.1097/JOM.0000000000000776>

We found associations between burn pit emissions exposure and higher incidence of post-deployment self-reported respiratory and cardiovascular conditions, but these findings should be interpreted with caution because the surrogate measurements of burn pit emissions exposure in this analysis may not reflect individual exposure levels.

Falvo, M. J., Abraham, J. H., Osinubi, O. Y., Klein, J. C., Sotolongo, A. M., Ndirangu, D., Patrick-DeLuca, L. A., & Helmer, D. A. (2016). **Bronchodilator Responsiveness and Airflow Limitation Are Associated With Deployment Length in Iraq and Afghanistan Veterans.** *Journal of occupational and environmental medicine*, 58(4), 325–328. <https://doi.org/10.1097/JOM.0000000000000675>

In our sample of post-9/11 veterans, longer deployment lengths were associated with significant bronchodilator responsiveness and a trend toward airflow limitation independent of tobacco use.

Falvo, M. J., Osinubi, O. Y., Sotolongo, A. M., & Helmer, D. A. (2015). **Airborne hazards exposure and respiratory health of Iraq and Afghanistan veterans.** *Epidemiologic reviews*, 37, 116–130. <https://doi.org/10.1093/epirev/mxu009>

In summary, published data based on case reports and retrospective cohort studies suggest a higher prevalence of respiratory symptoms and respiratory illness consistent with airway obstruction. However, the association between chronic lung disease and airborne hazards exposure requires further longitudinal research studies with objective pulmonary assessments.

Falvo, M. J., Bradley, M., & Brooks, S. M. (2014). **Is deployment an "exposure" in military personnel?** *Journal of occupational and environmental medicine*, 56(11), e139–e140. <https://doi.org/10.1097/JOM.0b013e3182941a43>

In this perspective, we consider whether deployment may be considered an exposure using an occupational medicine perspective. Specifically, we incorporate the Hill model of disease causality and discuss aspects of association.

Farmer, S. A., Nelin, T. D., Falvo, M. J., & Wold, L. E. (2014). **Ambient and household air pollution: complex triggers of disease.** *American journal of physiology. Heart and circulatory physiology*, 307(4), H467–H476. <https://doi.org/10.1152/ajpheart.00235.2014>

This review provides a summary of the detrimental effects of air pollution through examination of current animal, clinical, and epidemiological studies and exposure during three different periods: maternal (in utero), early life, and adulthood. Additionally, we recommend future lines of research while suggesting conceivable strategies to curb exposure to indoor and outdoor air pollutants.

Falvo, M. J., Serrador, J. M., McAndrew, L. M., Chandler, H. K., Lu, S. E., & Quigley, K. S. (2012). **A retrospective cohort study of U.S. service members returning from Afghanistan and Iraq: is physical health worsening over time?** *BMC public health*, 12, 1124. <https://doi.org/10.1186/1471-2458-12-1124>

In our clinical sample, the longer the duration between return from deployment and their visit to our clinic, the worse the Veteran's physical health even after adjusting for PTSD. Additionally, a decline is also present in a military community sample of OEF/OIF veterans. These data suggest that, as time since deployment length increases, physical health may deteriorate for some veterans.