A Systematic Review of Human Studies Assessing the Health Effects of Kerosene-Based Jet Fuels and Products Across Diverse Populations and Settings

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NASEM Clinical Follow-Up and Care for Those Impacted by the JP-5 Releases at Red Hill Webinar Series

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Presentation Plan

- Petroleum hydrocarbon pollution
- Jet fuel & kerosene - composition, usage, research
- Scope & objective
- Steps taken to perform review
- Characteristics of included studies
- Health effects observed
- Alignment with previous research
- Looking ahead

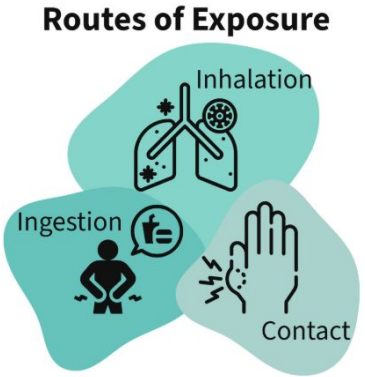
Petroleum hydrocarbons are the most prevalent environmental contaminants globally

- **Petroleum hydrocarbons** - family of hundreds of crude-oil-derived chemical compounds
- **Global petroleum consumption** 97.3 million barrels per day (b/d) in 2021
  - Extensive uses in transportation, heating, and industry
- **Environmental pollution** through refinement of crude oil, operational failures, leakages, spills, and as byproducts from commercial or private uses

Agency for Toxic Substances and Disease Registry (ATSDR). (1999, September). *Toxicological profile for Total Petroleum Hydrocarbons (TPH)*.; Kuppusamy, S., Maddela, N. R., Megharaj, M., & Venkateswarlu, K. (2020). *Total Petroleum Hydrocarbons: Environmental Fate, Toxicity, and Remediation*. Springer International Publishing. https://doi.org/10.1007/978-3-030-24035-6; Truskewycz, A., Gundry, T. D., Khudur, L. S., Kolobaric, A., Taha, M., Aburto-Medina, A., Ball, A. S., & Shahsavari, E. (2019). Petroleum Hydrocarbon Contamination in Terrestrial Ecosystems—Fate and Microbial Responses. *Molecules*, *24*(18), 3400. https://doi.org/10.3390/molecules24183400.; U.S. Energy Information Administration (EIA). (2023, August 22). *Use of oil—U.S. Energy Information Administration (EIA)*. U.S. Energy Information Administration.

Petroleum Hydrocarbon Exposure

- Enter the body when inhaled, ingested or in contact with skin
  - Can impact various organ systems depending on metabolism and distribution



- **Health effects = nature of compound + duration + dose**

Agency for Toxic Substances and Disease Registry (ATSDR). (1999, September). *Toxicological profile for Total Petroleum Hydrocarbons (TPH)*

Jet Fuel Pollution

- United States (US) - daily petroleum consumption averaged ~**20.3 million b/d** in 2022
  - 67% went to transportation including the **1.6 million barrels of kerosene-type jet fuels** (e.g., Jet A, JP-5 and JP-8)
    - **8%** of total daily petroleum consumption in the US
- Jet fuels enter the environment during routine processes such as storage, handling and transportation, in-flight jettisoning, as well as accidental spills or leaks

Agency for Toxic Substances and Disease Registry (ATSDR). (2017, March). *JP-5, JP-8, and Jet A | Toxicological Profile | ATSDR.*; U.S. Energy Information Administration (EIA). (2023, August 22). *Use of oil—U.S. Energy Information Administration (EIA)*. U.S. Energy Information Administration.

Composition, Use and Existing Research: Jet Fuel

- Most jet fuels kerosene-based; **varying proportions** by fuel type
  - Contain **performance additives** and agents to prevent icing, static buildup, corrosion, and bacterial growth
- Commercial aviation: Jet A (continental US flights) & Jet A-1 (international)
  - Jet A also used by US Air Force
- Military jet propellants (JP): JP-4, 5, 6, 7, 8
- JP-5 and JP-8 = 99.5% kerosene-based aircraft fuels used by US military
  - JP-8 most widely used by US military for air and ground operations
  - JP-5 used by the US navy aboard aircraft carriers

Agency for Toxic Substances and Disease Registry (ATSDR). (2017, March). *JP-5, JP-8, and Jet A | Toxicological Profile | ATSDR*.; Kuppusamy, S., Maddela, N. R., Megharaj, M., & Venkateswarlu, K. (2020). *Total Petroleum Hydrocarbons: Environmental Fate, Toxicity, and Remediation*. Springer International Publishing. https://doi.org/10.1007/978-3-030-24035-6; Ritchie, G., Still, K., Rossi, J., Bekkedal, M., Bobb, A., & Arfsten, D. (2003). Biological and health effects of exposure to kerosene-based jet fuels and performance additives. *Journal of Toxicology and Environmental Health. Part B, Critical Reviews*, *6*(4), 357–451. https://doi.org/10.1080/10937400306473

Composition, Use and Existing Research: Jet Fuel

- Largest chemical exposure among U.S. military personnel, frequent occupational exposure in non-military settings
  - Fueling, transporting, routine maintenance of aircraft = increased risk
- Bulk of research consists of **animal** or ***in vitro*** studies
- Limited human studies:
  - **Occupational** exposure
  - **Males** of working age
    - Healthy worker effect
  - **Dermal** and **inhalation** exposures
  - Little distinction between **pre- vs. post-combustion**

Agency for Toxic Substances and Disease Registry (ATSDR). (2017, March). *JP-5, JP-8, and Jet A | Toxicological Profile | ATSDR*.; Kuppusamy, S., Maddela, N. R., Megharaj, M., & Venkateswarlu, K. (2020). *Total Petroleum Hydrocarbons: Environmental Fate, Toxicity, and Remediation*. Springer International Publishing. https://doi.org/10.1007/978-3-030-24035-6; Ritchie, G., Still, K., Rossi, J., Bekkedal, M., Bobb, A., & Arfsten, D. (2003). Biological and health effects of exposure to kerosene-based jet fuels and performance additives. *Journal of Toxicology and Environmental Health. Part B, Critical Reviews*, *6*(4), 357–451. https://doi.org/10.1080/10937400306473

Composition, Use and Existing Research: Kerosene

- Petroleum-derived oil
  - Fuel oil no. 1, paraffin, paraffin oil, lamp oil
- Used as household fuel, transportation & in lubricants and pesticides
- Fuel for cooking and lighting in low- & middle-income countries (LMIC)
  - Studies often assess household **air pollution**
  - Limited research on **unburned kerosene**
    - Reports on poisoning among children of LMICs

Limitations of Current Research

- Occupational scope of previous reviews
  - **Residential, community** settings?
- **Oral** vs. dermal & inhalation exposures
- Exposures to **raw, unburned** fuel
- Understudied populations (**women, children, older adults**)

Recent contamination events highlight need for further research

Methods

Guiding Research Question (PECO):

"What are the known and/or potential health effects of exposure (oral, dermal, and inhalation) to **pre-combustion** forms of **kerosene-based jet fuel**, and other **kerosene** products, in **humans** across **all** exposure **settings** and **population groups**?"

- Protocol development
  - Eligibility criteria
  - Search strategies
- PRISMA guidelines

PROSPERO Registration

Eligibility Criteria

a) assess the association between oral, dermal and/or inhalation exposures to **pre-combustion** forms of kerosene-based jet fuel or other kerosene products, and health related effects in **humans**
b) be peer reviewed and an **original study**
c) be published between **2017 to 2024** in English, French, Dutch, Spanish or Portuguese
d) be **experimental, descriptive or observational in design**
e) conduct investigations ***in-vivo***

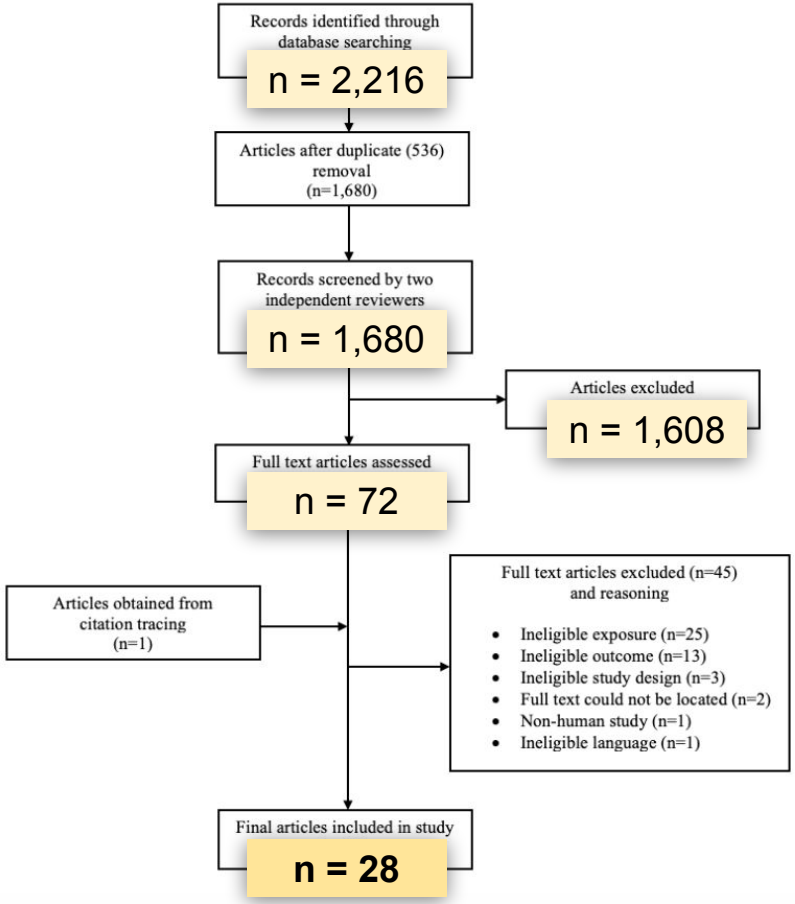
Search Strategies

(Jet fuel & Kerosene terms) AND (Health Effects terms)

Database	Search terms	Limitations	Output
PubMed	(("JP5 jet fuel" [Supplementary Concept] OR "S-8 fuel" [Supplementary Concept] OR "JP8 aviation fuel" [Supplementary Concept] OR "Kerosene"[Mesh] OR kerosene[Title/Abstract] OR "jet propellant"[Title/Abstract] OR "jet propellants"[Title/Abstract] OR "aviation fuel"[Title/Abstract] OR "aviation fuels"[Title/Abstract] OR "jet fuel"[Title/Abstract] OR "jet fuels"[Title/Abstract] OR "turbine fuel"[Title/Abstract] OR "turbine fuels"[Title/Abstract] OR "jet propulsion fuel"[Title/Abstract] OR "jet propulsion fuels"[Title/Abstract] OR "Jet A"[Title/Abstract] OR "Jet A-1"[Title/Abstract] OR "Jet B"[Title/Abstract] OR "JP-1"[Title/Abstract] OR "JP1"[Title/Abstract] OR "JP-2"[Title/Abstract] OR "JP2"[Title/Abstract] OR "JP-3"[Title/Abstract] OR "JP3"[Title/Abstract] OR "JP-4"[Title/Abstract] OR "JP4"[Title/Abstract] OR "JP-5"[Title/Abstract] OR "JP5"[Title/Abstract] OR "JP-6"[Title/Abstract] OR "JP6"[Title/Abstract] OR "JP-7"[Title/Abstract] OR "JP7"[Title/Abstract] OR "JP-8"[Title/Abstract] OR "JP8"[Title/Abstract] OR "zip fuel"[Title/Abstract] OR "zip fuels"[Title/Abstract] OR "JPTS"[Title/Abstract] OR "Jet Propellant Thermally Stable"[Title/Abstract] OR "TS-1"[Title/Abstract])) AND (("Diseases Category"[Mesh] OR "Psychiatry and Psychology Category"[Mesh] OR depression[Title/Abstract] OR "analysis"[Subheading] OR "epidemiology"[Subheading] OR "toxicity"[Subheading] OR "Toxicology"[Mesh] OR "injuries"[Subheading] OR "etiology"[Subheading] OR "Pathologic Processes"[Mesh] OR "physiology"[Subheading] OR Health[Title/Abstract] OR "health effect"[Title/Abstract] OR "health effects"[Title/Abstract] OR "adverse effect"[Title/Abstract] OR "adverse effects"[Title/Abstract] OR "side effect"[Title/Abstract] OR "side effects"[Title/Abstract] OR disease[Title/Abstract] OR morbidit*[Title/Abstract] OR mortalit*[Title/Abstract] OR incidence[Title/Abstract] OR prevalence[Title/Abstract] OR symptom[Title/Abstract] OR	Publication date: 2017-2024	862
	heart[Title/Abstract] OR skin[Title/Abstract] OR dermal[Title/Abstract] OR renal[Title/Abstract] OR cancer[Title/Abstract] OR lung[Title/Abstract] OR exposure[Title/Abstract] OR reproductive[Title/Abstract] OR genetic[Title/Abstract] OR imbalance[Title/Abstract] OR breath*[Title/Abstract] OR rash*[Title/Abstract] OR metabol*[Title/Abstract] OR pain[Title/Abstract] OR coordination[Title/Abstract] OR memory[Title/Abstract] OR fatigue[Title/Abstract] OR weak*[Title/Abstract]))		
Web of Science	(AB=(("Jet Propellant" OR "Jet Propellants" OR "Aviation Fuel" OR "Aviation Fuels" OR "Jet Fuel" OR "Jet Fuels" OR "turbine fuel" OR "turbine fuels" OR "jet propulsion fuel" OR "jet propulsion fuels" OR "Jet A" OR "Jet A-1" OR "Jet B" OR "JP-1" OR "JP1" OR "JP-2" OR "JP2" OR "JP-3" OR "JP3" OR "JP-4" OR "JP4" OR "JP5 jet fuel" OR "JP-5" OR "JP5" OR "JP-6" OR "JP6" OR "JP-7" OR "JP7" OR "S-8 fuel" OR "JP-8" OR "JP8" OR "JPTS" OR "Jet Propellant Thermally Stable" OR "TS-1" OR "zip fuel" OR "zip fuels" OR kerosene))) AND AB=(("adverse effect" OR "adverse effects" OR "side effect" OR "side effects" OR "long term effect" OR "long term effects" OR "acute effect" OR "acute effects" OR exposure OR health OR disease* OR illness* OR disorder OR mortalit* OR incidence OR prevalence OR "quality of life" OR depression OR poison* OR toxic* OR heart OR digest* OR reproduct* OR immun* OR metaboli* OR respirat* OR asthma OR bronchitis OR lung OR breath* OR skin OR renal OR cancer* OR memory OR eye* OR gene OR genetic OR mutation OR hormon* OR vision OR confusion OR diarrhea OR imbalance OR pregnancy OR male OR female OR enzymes))	Document type: Article, Early Access Publication date: 2017-01-01 to 2024-12-21	1,354

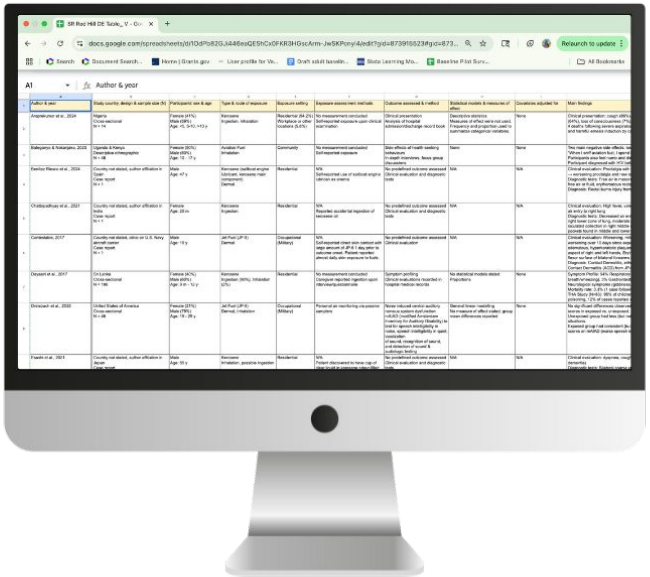
Article Selection Process

- Blind, independent screening
- Participation of three reviewers
- Consensus required to progress



Data Extraction

- First author, publication year, country of study
- Study design, sample size, age/sex of participants
- Exposure type, route, setting, assessment methods
- Health outcomes assessed & methods
- Statistical models, measures of effect, covariates adjusted for in statistical analyses
- Main findings applicable to the research question of review



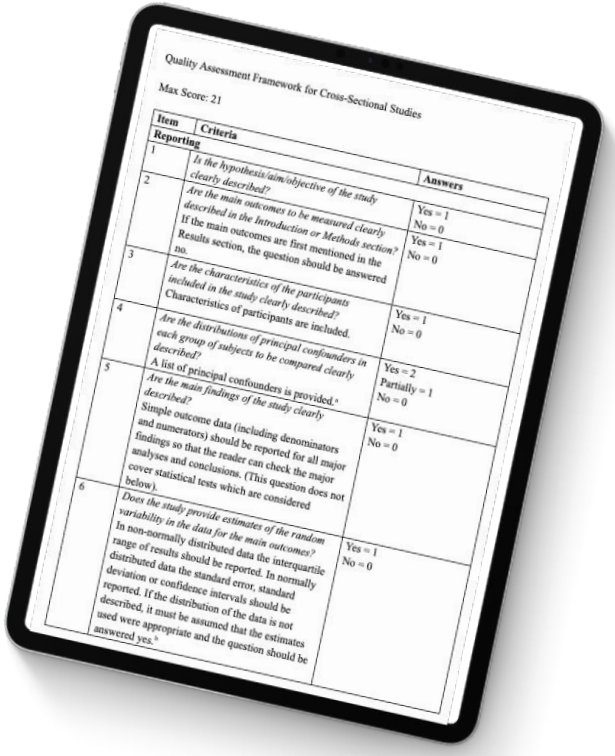
Conducted blind and independently by two reviewers

Quality Assessment

- **Four checklists** developed based on study design
  - Modified Downs & Black
  - Joanna Briggs
  - Previous review in the field
    (Carvajal et al., 2025)

- Conducted **blind and independently** by two reviewers
  - Consensus required to progress

- Informed **synthesis and interpretation** of evidence



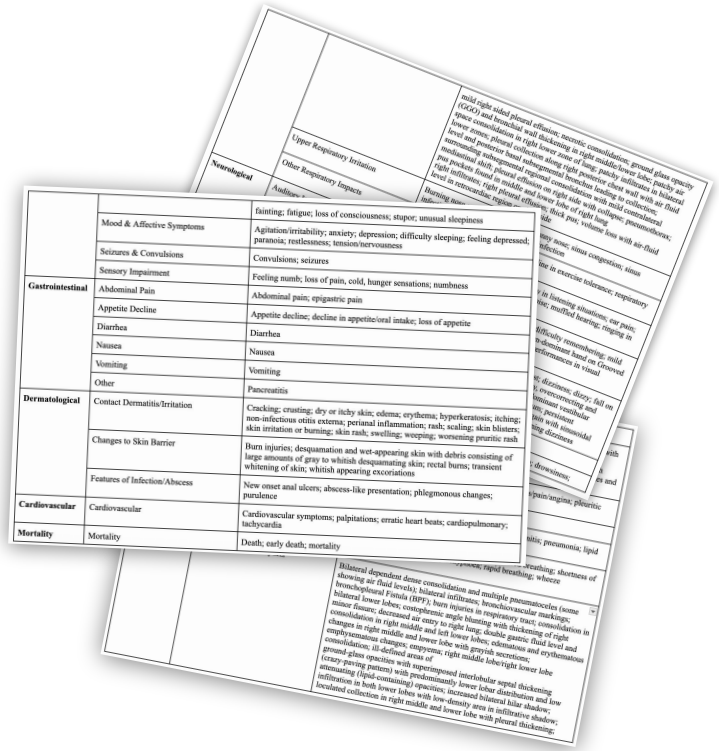
Quality Assessment Framework for Cross-Sectional Studies

Max Score: 21

Item	Criteria	Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	Yes = 1 No = 0
2	*Are the main outcomes to be measured clearly described in the Introduction or Methods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1 No = 0
3	*Are the characteristics of the participants included in the study clearly described?* Characteristics of participants are included.	Yes = 1 No = 0
4	*Are the distributions of principal confounders in each group of subjects to be compared clearly described?* A list of principal confounders is provided.[a]	Yes = 2 Partially = 1 No = 0
5	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).	Yes = 1 No = 0
6	*Does the study provide estimates of the random variability in the data for the main outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.[b]	Yes = 1 No = 0

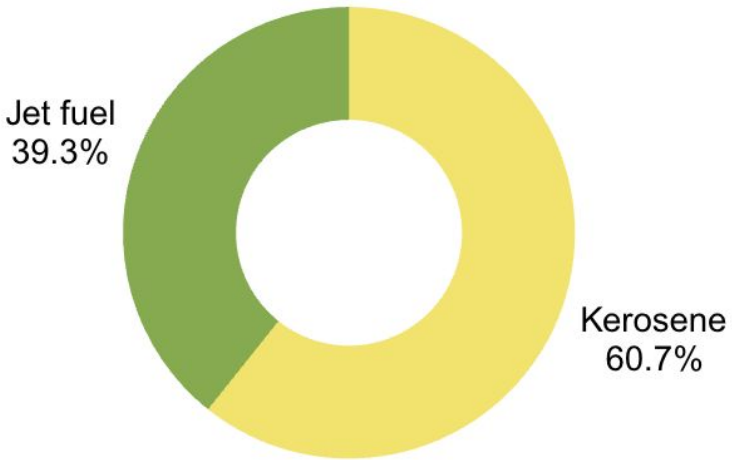
Analysis & Evaluation of Evidence

- Categorization of health effects by **bodily system** -> **clinical similarity**
- Binary coding
- Assessed **distribution of outcomes** via frequency counts
- Stratified by **exposure type**
- Stratified by **study quality** (good/excellent vs. lower quality) to assess consistency and robustness of findings



Characteristics of included studies

28 Included Studies (100%)



- Primarily **descriptive reports** (89%) of clinical evaluations
  - Case-reports
  - Case-series
  - Cross-sectional
- **3 analytical** studies
  - Jet fuel specific
    - Occupational
- **Self-reported** exposure (86%)

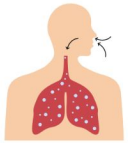
Characteristics of Kerosene-specific Studies

Characteristic	Kerosene (N=17) (%)
Exposure Route	
Oral	12 (71%)
Inhalation	5 (29%)
Dermal	2 (12%)
Exposure Duration	
Acute	17 (100%)
Chronic	0
Exposure Setting	
Residential	11 (65%)
Community	4 (24%)
Occupational (Non-military & military)	1 (6%)
Occupational (Non-military)	1 (6%)
Occupational (Military)	0
Not stated	5 (29%)
Age Group	
Children	10 (59%)
Infants	6 (35%)
Adults	4 (24%)
Older Adults	3 (18%)

- Ingestion (71%)
  - Inhalation (29%), Dermal (12%)
- Acute (100%)
  - Chronic (0)
- Residential (65%) & Community (24%)
  - Occupational (6%)
- Children (59%) and Infants (35%)
  - Adults (24%), Older Adults (18%)

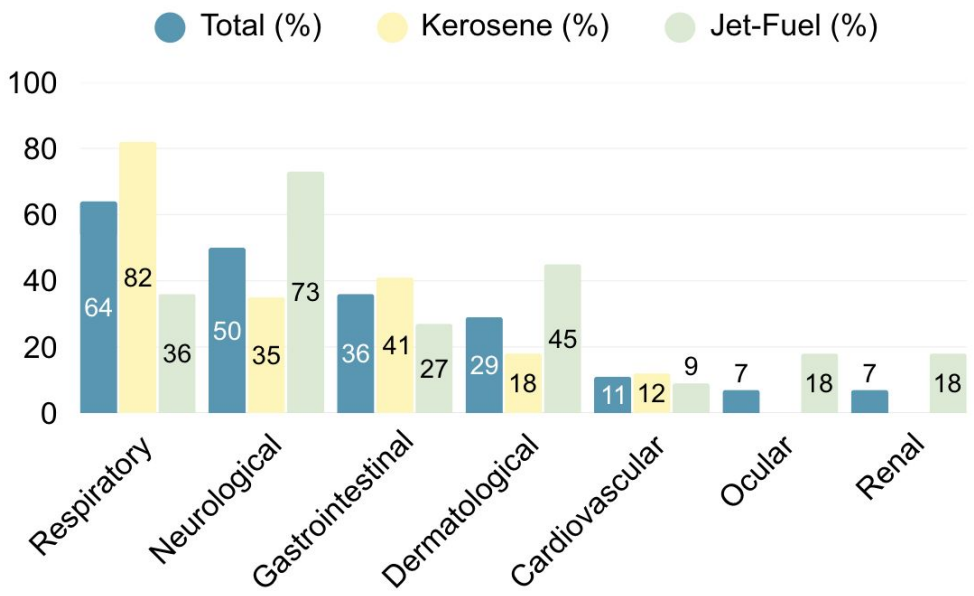
Characteristics of Jet Fuel-specific Studies

Characteristic	Jet Fuel (N=11) (%)
Exposure Route	
Oral	2 (18%)
Inhalation	9 (82%)
Dermal	8 (73%)
Exposure Duration	
Acute	1 (9%)
Chronic	10 (91%)
Exposure Setting	
Residential	1 (9%)
Community	2 (18%)
Occupational (Non-military & military)	10 (91%)
Occupational (Non-military)	2 (18%)
Occupational (Military)	9 (82%)
Not stated	0
Age Group	
Children	2 (18%)
Infants	1 (9%)
Adults	10 (91%)
Older Adults	1 (9%)



- Inhalation (82%), Dermal (73%)
  - Oral (18%)
- Chronic (91%)
  - Acute (9%)
- Occupational (91%), Military (82%)
  - Non-military (18%)
  - Community (18%), Residential (9%)
- Adults (91%)
  - Children (18%), Infants (9%), Older Adults (9%)

Health Effects of Included Studies



Affected Bodily System	Total	Jet Fuel	Kerosene
Respiratory	18 (64%)	4 (36%)	14 (82%)
Neurological	14 (50%)	8 (73%)	6 (35%)
Gastrointestinal	10 (36%)	3 (27%)	7 (41%)
Dermatological	8 (29%)	5 (45%)	3 (18%)
Cardiovascular	3 (11%)	1 (9%)	2 (12%)
Ocular	2 (7%)	2 (18%)	0
Renal	2 (7%)	2 (18%)	0

Cancer, endocrine, developmental, hepatic, immune, reproductive, musculoskeletal and metabolic outcomes **not identified**

Frequent Health Effects: Kerosene-specific Reports

Respiratory
(N=14, 82%)

Laboured breathing, infectious/inflammatory lung conditions, cough

- Tissue/mechanical impacts, abnormal breath sounds, chest discomfort*

Gastrointestinal
(N=7, 41%)

Vomiting

- Abdominal pain, pancreatitis*, nausea

Neurological
(N=6, 35%)

Impaired consciousness

- Cognitive function & processing*, seizures & convulsions, equilibrium & spatial disorientation, mood & affective symptoms

Frequent Health Effects: Jet Fuel-specific Reports

Neurological
(N=8, 73%)

Auditory impacts, cognitive function & processing
- Equilibrium & spatial disorientation*, head pain/discomfort, impaired consciousness

Dermatological
(N=5, 45%)

Contact dermatitis/irritation
- Changes to skin barrier*

Respiratory
(N=4, 36%)

Cough
- Chest discomfort, laboured breathing*

Exposure Context

Kerosene

- Acute
- Ingestion
- Residential & community

Respiratory Effects

Jet Fuel

- Chronic
- Inhalation & dermal
- Occupational settings

Neurological Effects

*Rate and extent of **TPH absorption** varies depending on **how** compounds enter the body*

Agency for Toxic Substances and Disease Registry (ATSDR). (1999, September). *Toxicological profile for Total Petroleum Hydrocarbons (TPH).*;

Alignment with Previous Findings

Respiratory (N=14, 82%)

Laboured breathing, infectious/inflammatory lung conditions, cough

- Tissue/mechanical impacts, abnormal breath sounds, chest discomfort

Previous reports of **kerosene ingestion in humans** (ATSDR, 2017, Ritchie et al., 2011)

- Pneumonitis, cough, dyspnea, pulmonary edema, lung infiltrates, tachypnea, pneumothorax

Alignment with Previous Findings

Neurological (N=8, 73%)	**Auditory impacts, cognitive function & processing** ○ Equilibrium & spatial disorientation, head pain/discomfort, impaired consciousness

- ATSDR, 1999, 2017 & Ritchie et al., 2011:
  - **Kerosene ingestion**: nervous system depression, lethargy, coma, drowsiness, convulsions, restlessness and irritability
  - **Animal studies**: lethargy, ototoxic hearing loss, central auditory dysfunction, and impaired learning in rats exposed to JP-8

Descriptive and analytical evidence align with animal studies

Health outcomes requiring longer latency periods not identified

Cancer, endocrine, developmental, hepatic, immune, reproductive, musculoskeletal and metabolic outcomes ***not identified***

ATSDR 1999, 2017:

Cancer

- Malignant lymphomas, skin cancer (dermal JP-5 exposure)
- Tumours of the uterus and vagina (kerosene ingestion)

Reproductive & Developmental

- Increased maternal deaths, decreased sperm motility, reduced fetal weight, decreased litter size, suppressed immune function in pups (Inhalation/ingestion JP-8)

Metabolic *several reports* of decreased body weight

- Male, fetal and pregnant rats (Ingestion/inhalation, JP-5 & JP-8)

Lack of long-term follow up needed vs. absence of risk

Possible Mechanisms of Toxicity

Jet Fuel (Jet A, JP-8) → TNF-α & CXCL8 (IL-8)

TNF-α & CXCL8 (IL-8) → Inflammatory processes across several organ systems

Jet Fuel (Jet A, JP-8) → **TNF-α & CXCL8 (IL-8)** → **Observed health effects** (respiratory, neurological, gastrointestinal, dermatological)

Allen, D. G., Riviere, J. E., & Monteiro-Riviere, N. A. (2000). Identification of early biomarkers of inflammation produced by keratinocytes exposed to jet fuels jet A, JP-8, and JP-8(100). J. Biochem. Mol. Toxicol; Lin, R.-L., Gu, Q. Khosravi, M., & Lee, L.-Y. (2017). Sustained sensitizing effects of tumor necrosis factor alpha on sensory nerves in lung and airways; Mukhopadhyay, S., Hoidal, J. R., & Mukherjee, T. K. (2006). Role of TNFα in pulmonary pathophysiology; Jatakanon, A., Uasuf, C., Maziak, W., Lim, S., Chung, K. F., & Barnes, P. J. (1999). Neutrophilic Inflammation in Severe Persistent Asthma;Arican, O., Aral, M., Sasmaz, S., & Ciragil, P. (2005). Serum Levels of TNF-α, IFN-γ, IL-6, IL-8, IL-12, IL-17, and IL-18 in Patients With Active Psoriasis and Correlation With Disease Severity; Cotton, J. A., Platnich, J. M., Muruve, D. A., Jijon, H. B., Buret, A. G., & Beck, P. L. (2016). Interleukin-8 in gastrointestinal inflammation and malignancy: Induction and clinical consequences; Montgomery, S. L., & Bowers, W. J. (2012). Tumor Necrosis Factor-alpha and the Roles it Plays in Homeostatic and Degenerative Processes Within the Central Nervous System.

Important Considerations

- **Availability & heterogeneity** of data
  - Fuel type, exposure route, outcomes, demographics…
  - Subgroup analysis
- **Descriptive evidence**
  - Lack of **confounder assessment**, co-occurring environmental contaminants likely
  - Limited **testing of associations & dose-response** relationships
  - Limited follow-up needed to observe **latent health outcomes**

Looking Ahead

- Further epidemiological studies (occupational & non-occupational)
- **Ingestion**-related exposure
- Inclusion of **women, children, older adults**
- Attention to **exposure context**
  - Quantification, characterization, dose, route, duration
- **Longitudinal** designs
- Assessment of **respiratory & neurological** effects
  - Physiological mechanisms behind these effects

Interested in learning more?

Scan the QR code to access our pre-print

Red Hill Registry Team

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- Netherlands Institute for Health Services Research
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