



National Institute of
Environmental Health Sciences

**PROTOCOL FOR EVIDENCE MAP OF
INFLAMMATION-BASED ATHEROSCLEROSIS ASSOCIATED
WITH ENVIRONMENTAL EXPOSURES**

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PROTOCOL TO EVALUATE THE EVIDENCE OF INFLAMMATION-BASED ATHEROSCLEROSIS ASSOCIATED WITH POLYCYCLIC AROMATIC HYDROCARBON EXPOSURE

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Summary: The National Institute of Environmental Health Sciences (NIEHS) is conducting a systematic review to evaluate the evidence for inflammation-based atherosclerosis associated with exposure to polycyclic aromatic hydrocarbons.

BACKGROUND AND SIGNIFICANCE

Background

Persistent inflammation from prolonged exposure to stimuli can lead to chronic inflammation, long-term elevation of inflammatory mediators, and tissue damage. Chronic inflammation can ultimately contribute to numerous health effects, including cardiovascular and pulmonary conditions, cancer, autoimmune diseases, and diabetes (Gorman et al. 2004, Zakyntinos and Pappa 2009, Donath and Shoelson 2011, Hanahan and Weinberg 2011, Wyss-Coray and Rogers 2012, Schwarze et al. 2013). A growing body of evidence suggests a role of environmental exposures in a wide range of diseases that involve inflammation, and that activation of an inflammatory pathway is mediated by three key biomarkers: fibrinogen, C-reactive protein (CRP), and interleukin-6 (IL-6) (Libby and King 2015, Ridker 2016). The extent to which environmental exposures affect this pathway to ultimately lead to cardiovascular effects remains unclear.

Cardiovascular disease encompasses many diseases of the heart or blood vessels, and an important underlying condition of cardiovascular disease is atherosclerosis (Goff et al. 2014). Atherosclerosis is the buildup of plaques (deposits of fat and other bloodborne substances) in the arterial walls that causes narrowing of the arteries and a subsequent restriction of blood flow. Atherosclerosis is a significant public health concern and is one of the dominant conditions underlying heart attack and stroke. A recent American Heart Association report found strong associations in the preclinical measures of atherosclerosis (e.g., carotid intima-media thickness) and mortality from cardiovascular disease (Benjamin et al. 2018). From an economic perspective, the cost of atherosclerosis-related diseases is significant. Cardiovascular disease in the United States alone was estimated to have cost \$555 billion in 2016, and this number is expected to double by 2035 (American Heart Association 2017). Although the exact cause of atherosclerosis is unclear, there is a well-established role of chronic inflammation in the disease process (Ross 1999, Pearson et al. 2003, Rosenfeld and Campbell 2011).

The purpose of this evidence map is to identify environmental exposures which may contribute to inflammation that ultimately leads to atherosclerosis.

Significance

The Division of Translational Toxicology (DTT) at National Institute of Environmental Health Sciences (NIEHS) will develop a systematic evidence map to identify environmental exposures associated with inflammation-based atherosclerosis. If the literature base is sufficient, this evidence map will inform the selection of relevant environmental exposure(s) to select for a systematic review of the evidence for an association between the selected exposure(s) and inflammation-based atherosclerosis.

OVERALL OBJECTIVE AND SPECIFIC AIMS

Objective

The first objective is to develop a systematic evidence map of relevant environmental exposures associated with development or exacerbation of atherosclerosis acting through an inflammation pathway and to identify the exposure that will be evaluated in the systematic review. The systematic evidence map will be based on guidance outlined in the Office of Health Assessment and Translation (OHAT) *Handbook for Conducting a Literature-based Health Assessment* (NTP, 2019).

Specific Aims

Scoping and problem formulation specific aims to identify environmental exposures:

- Identify literature that captures relevant environmental exposures associated with inflammation-based atherosclerosis
- Develop a systematic evidence map to identify and select an environmental exposure to move forward for a systematic review

Dependent on the extent and nature of the available evidence:

- Synthesize the evidence using data visualization to evaluate the both number of studies and environmental exposures relevant to inflammation-based atherosclerosis.

The systematic evidence map will identify the number of studies that examine inflammation-based atherosclerosis effects associated with acute or chronic environmental exposures from human studies across a broad range of study design types along with controlled exposure animal studies and mechanistic/*in vitro* studies based on the problem formulation efforts that identified these markers for inflammation as most relevant for atherosclerosis: (1) fibrinogen, (2) CRP, and (3) IL-6 (Libby and King 2015, Ridker 2016).

PECO Statement

PECO statements were developed as an aid to identify search terms and inclusion/exclusion criteria as appropriate for addressing the overall research question (inflammatory atherosclerosis from acute/chronic environmental exposure) for the environmental exposure (Higgins and Green 2011). The PECO statements are listed below for human (Table 1), animal (Table 2), and *in vitro*/mechanistic studies (Table 3).

Table 1. Human PECO (Population, Exposure, Comparator, and Outcome) Statement	
PECO Element	Evidence
Population	Humans without restriction as to age or sex, geographic location, or life stage at exposure or outcome assessment
Exposure	Acute or chronic environmental exposure based on: Known dose or concentration in an experimental protocol Diagnostic biomonitoring data (e.g., markers in plasma or urine) Environmental detection (e.g., air, soil) Corroboration by assessment of direct (in hospital, in clinic) or indirect observation of symptoms of atherosclerosis No restriction on whether exposure is accidental or intentional
Comparators	For controlled and uncontrolled studies, comparable populations not exposed to the environmental exposure; and case series-reports, no comparable populations
Outcomes	Atherosclerosis: The following outcome measures were considered for atherosclerosis and related diseases (e.g., coronary heart disease, carotid artery disease, peripheral artery disease, and chronic kidney disease): Fatal events (e.g., all-cause mortality, cardiovascular disease deaths, and other vascular deaths) Non-fatal events (e.g., acute coronary syndromes such as myocardial infarction, unstable angina pectoris, and cerebrovascular events such as stroke and aneurysm) Direct measurements of disease severity (e.g., coronary angiograms; digital subtraction angiograms for peripheral arterial disease; carotid intima-media thickness) Indirect measurements of disease severity (e.g., ankle-brachial pressure index, limb weakness, walking distance for claudicants) Inflammation: The following outcome measures were considered for inflammation: <ul style="list-style-type: none"> • Biomarkers of inflammation (e.g., cytokines, chemokines, eicosanoids, and prostanoids) • Inflammatory gene expression of fibrinogen, CRP, and IL-6 • Immune response from clotting factors (e.g., platelets), leukocyte infiltrate, differential white blood cells, and immunophenotyping (e.g., T cells, myeloid)

Table 2. Animal PECO (Population, Exposure, Comparator, and Outcome) Statement	
PECO Element	Evidence
Population	Without restriction as to species, age, sex, or life stage at exposure or outcome assessment
Exposure	Acute or chronic environmental exposure based on administered dose or concentration or biomonitoring data (e.g., urine, blood, or other specimens)
Comparators	Comparable untreated animal subjects or animals exposed to vehicle-only treatment
Outcomes	<p>Atherosclerosis: The following outcome measures were considered for atherosclerosis and related diseases (e.g., coronary artery disease, carotid artery disease, peripheral artery disease, and chronic kidney disease):</p> <p>Mortality</p> <p>Non-fatal events including acute coronary syndromes such as myocardial infarction, unstable angina pectoris, and cerebrovascular events such as stroke</p> <p>Effects on direct measurement of disease severity (e.g., artery/aorta lesion area/volume; aortic calcification; carotid intima-media thickness, coronary artery calcium; score, brachial artery index)</p> <p>Indirect tests of disease severity</p> <p>Inflammation: The following outcome measures were considered for inflammation:</p> <p>Biomarkers of inflammation (e.g., cytokines, chemokines, eicosanoids, and prostanoids)</p> <p>Inflammatory gene expression of fibrinogen, CRP, and IL-6</p> <p>Immune response from clotting factors (e.g., platelets), leukocyte infiltrate, differential white blood cells, and immunophenotyping (e.g., T cells, myeloid)</p>

Table 3. <i>In Vitro</i>/Mechanistic PECO (Population, Exposure, Comparator, and Outcome) Statement	
PECO Element	Evidence
Population	Human or animal cells, tissues, or model systems with <i>in vitro</i> exposure regimens
Exposure	Environmental exposures based on administered dose or concentration
Comparators	Comparable cells or tissues exposed to vehicle-only treatment or untreated controls
Outcomes	<p>Inflammation: The following outcome measures were considered for inflammation:</p> <ul style="list-style-type: none"> • Biomarkers of inflammation (e.g., cytokines, chemokines, eicosanoids, and prostanoids) • Inflammatory gene expression of fibrinogen, CRP, and IL-6 • Immune response from clotting factors (e.g., platelets), leukocyte infiltrate, differential white blood cells, and immunophenotyping (e.g., T cells, myeloid)

The overall objective, PECO statements, and strategy to synthesize study results were based on a series of problem formulation steps beginning with detailed input from scientific and clinical experts with backgrounds in toxicology, atherosclerosis, and systematic review.

METHODS

Step 1. Problem Formulation

Nomination History

OHAT proposes to examine the evidence that environmental substances contribute to inflammation that ultimately leads to atherosclerosis and to identify markers of the inflammation involved. This evaluation concept stems from discussions with the NIEHS Strategic Plan Cross-Divisional Implementation Planning Committee on Inflammation. The committee is keenly interested in work that would contribute to the identification of markers of environmentally induced inflammation and has identified the need for an evaluation of the available evidence that environmental triggers of inflammation lead to atherosclerosis.

The proposed focus for this evaluation is on a single inflammation-based health effect—atherosclerosis, or the buildup of plaques on artery walls leading to restricted blood flow—among a range of health effects potentially associated with inflammation resulting from exposure to environmental substances. The focus on a single health effect is proposed for several reasons: (1) to facilitate direct comparison of evidence supporting or opposing the role of environmental substances in promoting inflammation that leads to the health effect (in this case, atherosclerosis), (2) to identify and evaluate the evidence for specific markers of inflammation linked to the health effect, and (3) to select a health effect with a manageable database of relevant studies.

In addition to discussion with NIEHS/NTP scientists with expertise on inflammation and atherosclerosis, OHAT has solicited input from scientists at other federal agencies working on inflammation as well as atherosclerosis health effects, including scientists at the Environmental Protection Agency (EPA), National Heart, Lung, and Blood Institute (NHLBI), and the National Institute for Occupational Safety and Health (NIOSH).

Scoping of Inflammation-based Atherosclerosis Literature to Identify Relevant Exposures

Several environmental exposures have reported associations with atherosclerosis. These exposures include bisphenol A (BPA), diesel exhaust particles, particulate matter, persistent organic pollutants (POPs), phthalates, metals, and second-hand tobacco smoke (Brook and Rajagopalan 2010, Kallio et al. 2010, Lind and Lind 2011, Lind et al. 2012, Schwarze et al. 2013). For many of the xenobiotics, there is evidence for an association with both inflammation and atherosclerosis (Munzel et al. 2017).

Step 2. Search and Select Studies for Inclusion

Searching electronic databases

A literature search strategy was developed to identify all relevant records related to inflammation-based atherosclerosis and to identify potential environmental exposures that could be evaluated in a full systematic review. The search strategy utilized terms related to atherosclerosis, inflammation, and the three key biomarkers of inflammation (fibrinogen, CRP, and IL-6) identified by subject matter experts. In addition, a comprehensive list of terms related to environmental exposures was used to capture relevant exposures. A detailed list of all search terms used to identify relevant environmental exposures associated with inflammation-based atherosclerosis is listed in Appendix 1. The search was implemented on 2017-08-17 in six databases (full details of the search strategies are presented in Appendix 1).

- Cochrane Library and DARE

- Embase
- PubMed
- Scopus
- Toxline
- Web of Science

Searches will not be restricted by publication date. No language restrictions will be applied.

Selection criteria for the evidence

Once retrieved from the various databases, results were uploaded into SWIFT Active Screener (<https://www.sciome.com/swift-activescreener/>), an interactive software program that utilizes active machine learning technologies to prioritize results based on user-defined inclusion/exclusion criteria. Studies will be screened for inclusion using a structured form in SWIFT-Active Screener, a machine learning software program used to priority-rank studies for screening. SWIFT-Active Screener employs active learning to incorporate user feedback during the screening process to refine a statistical model that continually ranks the remaining studies according to their likelihood for inclusion. In addition, the software includes a statistical algorithm to estimate predicted recall (percent of truly relevant studies identified) while users work, thus providing a statistical basis for a decision about when to stop screening (Miller et al. 2016). The title and abstract screen will be stopped once the statistical algorithm in SWIFT-Active Screener estimates $\geq 98\%$ predicted recall. Two members of the review team will independently screen each title and abstract of the search results to identify studies that meet eligibility criteria. For citations with no abstract or non-English abstracts the articles will be excluded.

Development of the Systematic Evidence Map to Identify Relevant Exposures

Relevant studies will be uploaded and categorized into DistillerSR® (Evidence Partners, Ottawa, CA), a web-based, systematic review software program with structured forms and a searchable database of screening results. This information will then be used to generate a systematic evidence map to visualize the study characteristics of the body of literature using Tableau (Tableau Software, Seattle, USA) and to identify environmental exposures that could likely support a full systematic review.

The evidence map will be posted at the NIEHS website for this project once screening is completed. The results of the literature search will be presented in an interactive adaptation of a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram (<https://www.bmj.com/content/372/bmj.n71>) called an Interactive Reference Flow (I-REF) diagram.

REFERENCES

- American Heart Association (American Heart Association). 2017. *Cardiovascular disease: A costly burden for America, projections through 2035*. Washington DC. Available: <https://healthmetrics.heart.org/wp-content/uploads/2017/10/Cardiovascular-Disease-A-Costly-Burden.pdf>.
- Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, Chiuve SE, Cushman M, Delling FN, Deo R. 2018. Heart disease and stroke statistics—2018 update: A report from the American Heart Association. *Circulation* 137(12): e67-e492.
- Brook RD, Rajagopalan S. 2010. Particulate matter air pollution and atherosclerosis. *Curr Atheroscler Rep* 12(5): 291-300.
- Donath MY, Shoelson SE. 2011. Type 2 diabetes as an inflammatory disease. *Nature Reviews Immunology* 11(2): 98-107.
- Goff DC, Jr., Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, Greenland P, Lackland DT, Levy D, O'Donnell CJ, Robinson JG, Schwartz JS, Shero ST, Smith SC, Jr., Sorlie P, Stone NJ, Wilson PW, Jordan HS, Nevo L, Wnek J, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, DeMets D, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellke FW, Shen WK, Smith SC, Jr., Tomaselli GF. 2014. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 129(25 Suppl 2): S49-73.
- Gorman C, Park A, Dell K. 2004. The secret killer. Inflammation: The fires within. *TIME Magazine*.
- Hanahan D, Weinberg RA. 2011. Hallmarks of cancer: The next generation. *Cell* 144(5): 646-674.
- Higgins J, Green S. 2011. *Cochrane handbook for systematic reviews of interventions. Version 5.1. 0 [updated March 2011]*: The Cochrane Collaboration.
- Kallio K, Jokinen E, Saarinen M, Hamalainen M, Volanen I, Kaitosaari T, Ronnema T, Viikari J, Raitakari OT, Simell O. 2010. Arterial intima-media thickness, endothelial function, and apolipoproteins in adolescents frequently exposed to tobacco smoke. *Circulation: Cardiovascular Quality and Outcomes* 3(2): 196-203.
- Libby P, King K. 2015. Biomarkers: A challenging conundrum in cardiovascular disease. *Arteriosclerosis Thrombosis and Vascular Biology* 35(12): 2491-2495.
- Lind PM, Lind L. 2011. Circulating levels of bisphenol A and phthalates are related to carotid atherosclerosis in the elderly. *Atherosclerosis* 218(1): 207-213.
- Lind PM, van Bavel B, Salihovic S, Lind L. 2012. Circulating levels of persistent organic pollutants (POPs) and carotid atherosclerosis in the elderly. *Environmental Health Perspectives* 120(1): 38-43.
- Munzel T, Sorensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen LC, Brook RD, Rajagopalan S. 2017. Environmental stressors and cardio-metabolic disease: Part I-epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. *Eur Heart J* 38(8): 550-556.
- NTP (National Toxicology Program). 2019. *Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration*. Research Triangle Park.
- Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, 3rd, Criqui M, Fadl YY, Fortmann SP, Hong Y, Myers GL, Rifai N, Smith SC, Jr., Taubert K, Tracy RP, Vinicor F. 2003. Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation* 107(3): 499-511.
- Ridker PM. 2016. From C-Reactive Protein to Interleukin-6 to Interleukin-1: Moving Upstream To Identify Novel Targets for Atheroprotection. *Circulation Research* 118(1): 145-156.

- Rosenfeld ME, Campbell LA. 2011. Pathogens and atherosclerosis: Update on the potential contribution of multiple infectious organisms to the pathogenesis of atherosclerosis. *Thrombosis and Haemostasis* 106(5): 858-867.
- Ross R. 1999. Atherosclerosis--an inflammatory disease. *New England Journal of Medicine* 340(2): 115-126.
- Schwarze PE, Totlandsdal AI, Lag M, Refsnes M, Holme JA, Ovrevik J. 2013. Inflammation-related effects of diesel engine exhaust particles: Studies on lung cells in vitro. *Biomed Res Int* 2013: 685142.
- Wyss-Coray T, Rogers J. 2012. Inflammation in Alzheimer disease-a brief review of the basic science and clinical literature. *Cold Spring Harbor Perspectives in Medicine* 2(1): a006346.
- Zakynthinos E, Pappa N. 2009. Inflammatory biomarkers in coronary artery disease. *J Cardiol* 53(3): 317-333.

ABOUT THE PROTOCOL

Contributors

Systematic Review Subcommittee Team

The Systematic Review Subcommittee teams will be composed of federal staff and contractor staff. Federal staff members will do a self-evaluation for conflict of interest. Epidemiologists and toxicologists on this evaluation team should have at least three years of experience and/or training in reviewing studies, including summarizing studies and critical review (e.g., assessing study quality and interpreting findings). Experience in evaluating toxicological or clinical studies involving inflammation and/or atherosclerosis will be preferred. Team members should have at least a master's degree or equivalent in epidemiology, toxicology, translational development of novel compounds, or a related field.

Name	Affiliation
Andrew A. Rooney, Ph.D.	NIEHS, DTT, IHAB, Project co-lead
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Contract Support

Contractors listed below are anticipated to provide support necessary to complete the literature searches, study selection, data extraction, and risk-of-bias assessment.

Name	Affiliation
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Technical Advisors

Technical advisors will be outside experts retained on an as-needed basis to provide individual advice to the Systematic Review Subcommittee and analysts for a specific topic. The technical advisors will be selected for their experience with inflammation-based atherosclerosis and/or relevant environmental

exposures, and systematic review procedures. Service as a technical advisor will not necessarily indicate that an advisor has read the entire protocol or endorses the final document.

Name	Affiliation
Dr. Paul M. Ridker	Harvard Medical School
Dr. Peter Libby	Harvard Medical School
Dr. Wayne Cascio	U.S. Environmental Protection Agency

Sources of Support

[None]

Protocol History and Revisions

Date	Activity or Revision
May 02, 2019	Draft date
June 16, 2023	Internal review and revision (editorial)
July 7, 2023	Posting

APPENDICES

Appendix 1. Evidence Map Literature Search Strategy

Evidence Map: Literature Search Strategy	
Database	Search Terms
Cochrane Library	<p>Note: Cochrane search only includes atherosclerosis, inflammation, and biomarker terms</p> <p>((artery OR renal heart OR angina OR arrhythmia OR arrhythmias) AND plaque) OR Arteriosclerosis OR ((arterial OR carotid OR coronary) AND plaque) OR Atherogenesis OR atheroma OR atheromas OR Atheroscleroses OR Atherosclerosis OR Atherosclerotic OR fatty-streak OR fatty-streaks OR fibroatheroma OR fibroatheromas OR foam-cell OR foam-cells OR Peripheral-Arterial-Disease OR Peripheral-Arterial-Diseases OR Peripheral-Artery-Disease OR Peripheral-Artery-Diseases OR proatherogen* OR pro-atherogen*)</p> <p>AND</p> <p>(abscess OR acute-phase-reaction OR acute-phase-response OR Acute-phase-state OR cellulitis OR Empyema OR Sepsis-syndrome OR Sepsis-syndromes OR Serositis OR Suppuration OR Systemic-Inflammatory-Response-Syndrome OR anti-inflammation OR anti-inflammatory OR inflamed OR Inflammation OR inflammatory OR proinflammatory OR proinflammation OR pro-inflammatory OR pro-inflammation)</p> <p>AND</p> <p>(B-Cell-Differentiation-Factor OR B-Cell-Stimulatory-Factor-2 OR BSF-2 OR Coagulation-Factor-I OR C-reactive-Protein OR CRP OR Factor-I OR Fibrinogen OR Hepatocyte-Stimulating-Factor OR Hybridoma-Growth-Factor OR IFN-beta-2 OR IL6 OR IL-6 OR Interferon-beta-2 OR Interleukin-6 OR MGI-2 OR Myeloid-Differentiation-Inducing-Protein OR Plasmacytoma-Growth-Factor)</p>
Embase	<p>((('arteries':ti,ab OR 'artery':ti,ab OR 'arterial':ti,ab OR 'carotid':ti,ab OR 'coronary':ti,ab OR 'heart':ti,ab OR 'peripheral':ti,ab OR 'renal':ti,ab OR 'stenosis':ti,ab) AND 'plaque*':ti,ab) OR 'Atherogenesis':ti,ab OR 'atheroma*':ti,ab OR 'Atheroscleroses':ti,ab OR 'Atherosclerosis':ti,ab OR 'Atherosclerotic-plaque*':ti,ab OR 'fatty-streak*':ti,ab OR 'fibroatheroma*':ti,ab OR 'foam-cell*':ti,ab OR 'Peripheral-Arterial-Disease*':ti,ab OR 'Peripheral-Artery-Disease*':ti,ab OR 'proatherogen*':ti,ab OR 'pro-atherogen*':ti,ab OR 'Atherogenesis'/exp OR 'atheroma'/exp OR 'atheromatosis'/exp OR 'Atherosclerosis'/exp OR 'Atherosclerotic-plaque'/exp OR 'fatty-streak'/exp OR 'fibroatheroma'/exp OR 'foam-cell'/exp OR 'peripheral-arterial-disease'/exp)</p> <p>AND</p> <p>('abscess':ti,ab OR 'acute-phase-reaction':ti,ab OR 'acute-phase-response':ti,ab OR 'Acute-phase-state':ti,ab OR 'cellulitis':ti,ab OR 'Empyema':ti,ab OR 'Sepsis-syndrome':ti,ab OR 'Sepsis-syndromes':ti,ab OR 'Serositis':ti,ab OR 'Suppuration':ti,ab OR 'Systemic-Inflammatory-Response-Syndrome':ti,ab OR 'anti-inflammat*':ti,ab OR 'inflamed':ti,ab OR 'Inflammat*':ti,ab OR 'inflammation-mediators':ti,ab OR 'proinflammat*':ti,ab OR 'pro-inflammat*':ti,ab OR 'abscess'/exp OR 'acute-phase-response'/exp OR 'cellulitis'/exp OR</p>

Evidence Map: Literature Search Strategy	
Database	Search Terms
	<p>'Empyema'/exp OR 'Suppuration'/exp OR 'Systemic-Inflammatory-Response-Syndrome'/exp OR 'Inflammation '/exp)</p> <p>AND</p> <p>('B-Cell-Differentiation-Factor':ti,ab OR 'B-Cell-Stimulatory-Factor-2':ti,ab OR 'BSF-2':ti,ab OR 'Coagulation-Factor-I':ti,ab OR 'C-reactive-Protein':ti,ab OR 'CRP':ti,ab OR 'Factor-I':ti,ab OR 'Fibrinogen':ti,ab OR 'Hepatocyte-Stimulating-Factor':ti,ab OR 'Hybridoma-Growth-Factor':ti,ab OR 'IFN-beta-2':ti,ab OR 'IL6':ti,ab OR 'IL-6':ti,ab OR 'Interferon-beta-2':ti,ab OR 'Interleukin-6':ti,ab OR 'MGI-2':ti,ab OR 'Myeloid-Differentiation-Inducing-Protein':ti,ab OR 'Plasmacytoma-Growth-Factor':ti,ab OR 'gamma-Fibrinogen'/exp OR 'C-reactive-Protein'/exp OR 'Fibrinogen'/exp OR 'Interleukin-6'/exp)</p> <p>AND</p> <p>('1,3-butadiene':ti,ab OR "1,3-butadiene"/exp OR "2,3,7,8-tetrachlorodibenzo-p-dioxin":ti,ab OR "2-bromopropane":ti,ab OR "2-bromopropane"/exp OR "2-propanol":ti,ab OR "2-propanol"/exp OR "3,4-benzopyrene":ti,ab OR "benzo(a)pyrene":ti,ab OR "benzo-a-pyrene":ti,ab OR "Bisphenol-A":ti,ab OR "N,N-diethyltoluamide":ti,ab OR "PM(10)":ti,ab OR "PM(2.5)":ti,ab OR "PM10":ti,ab OR "PM2.5":ti,ab OR (('air':ti,ab OR 'airborne':ti,ab OR 'coarse':ti,ab OR 'ultrafine':ti,ab OR 'fine':ti,ab) AND ('particle*':ti,ab OR 'particulate*':ti,ab)) OR (('air':ti,ab OR 'outdoor':ti,ab OR 'outdoors':ti,ab OR 'outside':ti,ab OR 'ambient':ti,ab OR 'pollut*':ti,ab OR 'emissions':ti,ab OR 'exhaust*':ti,ab) AND ('sulfur-dioxide':ti,ab OR 'sulfur-dioxide':ti,ab OR 'SO2':ti,ab OR 'ozone':ti,ab OR 'ozone':ti,ab OR 'O3':ti,ab OR 'hydrogen-sulfide':ti,ab OR 'hydrogen-sulfide':ti,ab OR 'H2S':ti,ab OR 'carbon-monoxide':ti,ab OR 'carbon-monoxide':ti,ab OR 'nitric-oxide':ti,ab OR 'nitrogen-oxide':ti,ab OR 'nitrogen-oxides':ti,ab OR 'nitrogen-dioxide':ti,ab OR 'nitrogen-dioxide':ti,ab OR 'NOx':ti,ab OR 'NO(x)':ti,ab OR 'NO2':ti,ab)) OR (('fire':ti,ab OR 'flame':ti,ab) AND 'retardant*':ti,ab) OR (('halogenated':ti,ab OR 'chlorinated':ti,ab OR 'brominated':ti,ab OR 'polybrominated':ti,ab) AND 'diphenyl-ethers':ti,ab) OR (('metal':ti,ab OR 'metals':ti,ab) AND 'lead':ti,ab) OR (('occupation':ti,ab OR 'occupational':ti,ab OR 'occupations':ti,ab OR 'workplace':ti,ab OR 'work-place':ti,ab OR 'work-related':ti,ab OR 'worker':ti,ab OR 'workers':ti,ab OR 'employee':ti,ab OR 'employees':ti,ab) AND ('exposure':ti,ab OR 'exposed':ti,ab OR 'chemical':ti,ab OR 'chemicals':ti,ab OR 'hazards':ti,ab OR 'hazard':ti,ab)) OR (('smoke':ti,ab OR 'smoking':ti,ab) AND ('cigarette':ti,ab OR 'cigarettes':ti,ab OR 'tobacco':ti,ab OR 'cigar':ti,ab OR 'cigars':ti,ab)) OR (('vehicle':ti,ab OR 'vehicles':ti,ab OR 'vehicular':ti,ab OR 'auto':ti,ab OR 'automobile':ti,ab OR 'automobiles':ti,ab OR 'autos':ti,ab OR 'bus':ti,ab OR 'buses':ti,ab OR 'car':ti,ab OR 'truck':ti,ab OR 'trucks':ti,ab OR 'engine':ti,ab OR 'cars':ti,ab OR 'traffic':ti,ab OR 'transport*':ti,ab) AND ('emissions':ti,ab OR 'exhaust':ti,ab OR 'fume':ti,ab OR 'fumes':ti,ab)) OR (('wood':ti,ab OR 'wood':ti,ab OR 'firewood':ti,ab OR 'biomass':ti,ab OR 'charcoal':ti,ab OR 'fuel':ti,ab OR 'fuels':ti,ab OR 'gas':ti,ab OR 'gasoline':ti,ab OR 'kerosene':ti,ab OR 'dung':ti,ab OR 'manure':ti,ab) AND ('smoke':ti,ab OR 'smoke':ti,ab OR 'smoking':ti,ab OR 'combust':ti,ab OR 'combusted':ti,ab OR 'combustible':ti,ab OR 'combustibles':ti,ab OR 'burned':ti,ab OR 'burn':ti,ab OR 'burning':ti,ab)) OR ('endocrine':ti,ab AND ('disrupt':ti,ab OR 'disruptor':ti,ab OR 'disruptors':ti,ab)) OR ('environment*':ti AND 'epigen*':ti) OR ('indoor':ti,ab AND ('air':ti,ab OR 'environment':ti,ab OR 'exposure':ti,ab OR 'pollution':ti,ab OR 'Smoke':ti,ab)) OR</p>

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	'acetone':ti,ab OR 'acetone'/exp OR 'agent-orange':ti,ab OR 'agrochemical*':ti,ab OR 'air-pollutant':ti,ab OR 'air-pollutant'/exp OR 'air-pollutants':ti,ab OR 'air-pollution':ti,ab OR 'air-pollution'/exp OR 'air-quality':ti,ab OR 'air-quality'/exp OR 'aldrin':ti,ab OR 'aldrin'/exp OR 'allergen'/exp OR 'allergen*':ti,ab OR 'Amitraz':ti,ab OR 'Amitraz'/exp OR 'aromatic-hydrocarbon'/exp OR 'aromatic-hydrocarbons':ti,ab OR 'arsenate*':ti,ab OR 'arsenic':ti,ab OR 'arsenic'/exp OR 'arsenical*':ti,ab OR 'arsenite*':ti,ab OR 'atrazine':ti,ab OR 'atrazine'/exp OR 'avermectin':ti,ab OR 'avermectin'/exp OR 'benzene':ti,ab OR 'benzene'/exp OR 'benzopyrene':ti,ab OR 'black-carbon':ti,ab OR 'black-carbon'/exp OR 'butyl-benzyl-phthalate':ti,ab OR 'butyl-phthalate':ti,ab OR 'cadmium':ti,ab OR 'cadmium'/exp OR 'captan':ti,ab OR 'captan'/exp OR 'carbaryl':ti,ab OR 'carbofuran':ti,ab OR 'carbofuran'/exp OR 'carbon-black':ti,ab OR 'carbon-black'/exp OR 'carbon-monoxide':ti,ab OR 'carbon-monoxide'/exp OR 'carcinogen':ti,ab OR 'carcinogen'/exp OR 'carcinogenic':ti,ab OR 'carcinogenicity'/exp OR 'carcinogens':ti,ab OR 'cardiotox*':ti,ab OR 'cardiotoxicity'/exp OR 'cardiotoxin'/exp OR 'Chemical-compound'/exp OR 'Chemical-compound*':ti,ab OR 'chemical-exposure*':ti,ab OR 'chemical-mixture*':ti,ab OR 'chemical-product*':ti,ab OR 'chemical-substance*':ti,ab OR 'chlordan':ti,ab OR 'chlordan'/exp OR 'chlorfenvinphos':ti,ab OR 'chlorinated-hydrocarbon'/exp OR 'chlorinated-hydrocarbons':ti,ab OR 'chlorobenzene'/exp OR 'chlorobenzene*':ti,ab OR 'chlorofluorocarbon'/exp OR 'chlorofluorocarbon*':ti,ab OR 'chlorpyrifos':ti,ab OR 'chlorpyrifos'/exp OR 'chromium':ti,ab OR 'chromium'/exp OR 'cigarette smoke'/exp OR 'cobalt':ti,ab OR 'cobalt'/exp OR 'cooker*':ti,ab OR 'cooking':ti,ab OR 'cooking'/exp OR 'cookstove*':ti,ab OR 'cook-stove*':ti,ab OR 'coumaphos':ti,ab OR 'cytotoxin'/exp OR 'cytotox*':ti,ab OR 'DDT':ti,ab OR 'deet':ti,ab OR 'dermotox*':ti,ab OR 'diazinon':ti,ab OR 'dibutyl-phthalate':ti,ab OR 'dichlorodiphenyltrichloroethane*':ti,ab OR 'dichlorophenyl-dichloroethylene':ti,ab OR 'dichlorvos':ti,ab OR 'dichlorvos'/exp OR 'dieldrin':ti,ab OR 'dieldrin'/exp OR 'diesel':ti,ab OR 'diethylstilbestrol':ti,ab OR 'diethylstilbestrol'/exp OR 'dimethyl-phthalate':ti,ab OR 'dioxane'/exp OR 'dioxane*':ti,ab OR 'dioxin'/exp OR 'dioxin*':ti,ab OR 'dust':ti,ab OR 'dust'/exp OR 'elemental-carbon':ti,ab OR 'elemental-carbon'/exp OR 'Endocrine-disrupt*':ti,ab OR 'Endocrine-disruptor'/exp OR 'endosulfan':ti,ab OR 'endosulfan'/exp OR 'endrin':ti,ab OR 'endrin'/exp OR 'Environmental-agent*':ti,ab OR 'environmental-chemical'/exp OR 'environmental-chemical*':ti,ab OR 'environmental-compound*':ti,ab OR 'environmental-contaminant*':ti,ab OR 'environmental-determinant*':ti,ab OR 'environmental-epigenetic*':ti,ab OR 'environmental-estrogen*':ti,ab OR 'environmental-exposure'/exp OR 'environmental-exposure*':ti,ab OR 'environmental-factor'/exp OR 'environmental-factor*':ti,ab OR 'environmental-influence*':ti,ab OR 'environmental-pollutant*':ti,ab OR 'environmental-pollution':ti,ab OR 'environmental-stress'/exp OR 'environmental-stress*':ti,ab OR 'fireplace*':ti,ab OR 'flame retardant'/exp OR 'Flame-retardant'/exp OR 'Flame-retardant*':ti,ab OR 'formaldehyde':ti,ab OR 'formaldehyde'/exp OR 'fossil-fuel'/exp OR 'fossil-fuel*':ti,ab OR 'fungicide'/exp OR 'fungicide*':ti,ab OR 'gasoline'/exp OR 'gasoline*':ti,ab OR 'hazardous-compound*':ti,ab OR 'hazardous-exposure*':ti,ab OR 'hazardous-mixture*':ti,ab OR 'hazardous-product*':ti,ab OR 'hazardous-substance*':ti,ab OR 'heater*':ti,ab OR 'heating':ti,ab OR 'heating'/exp OR 'heavy-metal':ti,ab OR 'heavy-metal'/exp OR 'heavy-metals':ti,ab OR 'heptachlor':ti,ab OR 'heptachlor'/exp OR 'herbicide'/exp OR 'herbicide*':ti,ab OR 'hydrogen-sulfide':ti,ab OR 'hydrogen-sulfide'/exp OR 'immunotox*':ti,ab OR 'immunotoxicity'/exp OR 'immunotoxin'/exp OR 'indoor air pollution'/exp OR 'indoors':ti,ab OR 'industrial-chemical'/exp OR 'industrial-chemical*':ti,ab OR 'industrial-compound*':ti,ab OR 'insecticide'/exp OR 'insecticide*':ti,ab OR 'irradiated':ti,ab OR 'lead'/exp OR 'linalool':ti,ab OR 'linalool'/exp OR 'malathion':ti,ab OR 'malathion'/exp OR 'Mercury':ti,ab OR 'Mercury'/exp OR 'metal'/exp

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	<p>OR 'metals':ti,ab OR 'methoxychlor':ti,ab OR 'methoxychlor'/exp OR 'Methylmercury':ti,ab OR 'Methylmercury'/exp OR 'mold':ti,ab OR 'motor-vehicle'/exp OR 'motor-vehicle*':ti,ab OR 'mutagen':ti,ab OR 'mutagenic':ti,ab OR 'mutagenic-agent'/exp OR 'mutagenicity'/exp OR 'mutagens':ti,ab OR 'nephrotox*':ti,ab OR 'nephrotoxicity'/exp OR 'neurotox*':ti,ab OR 'neurotoxicity'/exp OR 'Nickel':ti,ab OR 'Nickel'/exp OR 'nitrate'/exp OR 'nitrate*':ti,ab OR 'nitrogen-dioxide':ti,ab OR 'nitrogen-dioxide'/exp OR 'noxae':ti,ab OR 'organic-chlorine':ti,ab OR 'organic-solvent':ti,ab OR 'organic-solvent'/exp OR 'organochlorin*':ti,ab OR 'organochlorine insecticide'/exp OR 'organochlorine pesticide'/exp OR 'organophosphorus compound'/exp OR 'organophosphorus*':ti,ab OR 'organotin compound'/exp OR 'organotin*':ti,ab OR 'oven*':ti,ab OR 'ozone':ti,ab OR 'ozone'/exp OR 'PAHs':ti,ab OR 'paraben*':ti,ab OR 'paraquat':ti,ab OR 'paraquat'/exp OR 'parathion':ti,ab OR 'parathion'/exp OR 'particulate-matter':ti,ab OR 'particulate-matter'/exp OR 'passive-smoke':ti,ab OR 'passive-smoking':ti,ab OR 'passive-smoking'/exp OR 'PBDE*':ti,ab OR 'PCBs':ti,ab OR 'PCDE*':ti,ab OR 'pentachlorophenol':ti,ab OR 'pentachlorophenol'/exp OR 'perchlorate'/exp OR 'perchlorate*':ti,ab OR 'perfluorinat*':ti,ab OR 'permethrin':ti,ab OR 'permethrin'/exp OR 'persistent-organic-pollutant'/exp OR 'persistent-organic-pollutant*':ti,ab OR 'Pesticid*':ti,ab OR 'pesticide'/exp OR 'petrol*':ti,ab OR 'phthalate*':ti,ab OR 'phytoestrogen'/exp OR 'phytoestrogen*':ti,ab OR 'plasticizer'/exp OR 'plasticizer'/exp OR 'plasticizer*':ti,ab OR 'pollen':ti,ab OR 'pollen'/exp OR 'pollutant'/exp OR 'pollutant*':ti,ab OR 'pollution':ti,ab OR 'pollution'/exp OR 'polybrominated biphenyl'/exp OR 'polybrominated diphenyl ether'/exp OR 'polychlorinated biphenyl'/exp OR 'polychlorinated-biphenyl':ti,ab OR 'polychlorinated-biphenyls':ti,ab OR 'polychlorobiphenyl':ti,ab OR 'polycyclic-aromatic-hydrocarbons':ti,ab OR 'polycyclic-aromatic-hydrocarbons'/exp OR 'pyrethrin'/exp OR 'pyrethrin*':ti,ab OR 'radiation':ti,ab OR 'radiation'/exp OR 'radon':ti,ab OR 'radon'/exp OR 'repellent*':ti,ab OR 'rodenticide'/exp OR 'rodenticide*':ti,ab OR 'rotenone':ti,ab OR 'rotenone'/exp OR 'secondhand-smoke':ti,ab OR 'second-hand-smoke':ti,ab OR 'secondhand-smoking':ti,ab OR 'second-hand-smoking':ti,ab OR 'smog':ti,ab OR 'smog'/exp OR 'solvent'/exp OR 'solvent*':ti,ab OR 'soot':ti,ab OR 'soot'/exp OR 'spores':ti,ab OR 'stilbene-estrogen':ti,ab OR 'stilbestrol':ti,ab OR 'stove*':ti,ab OR 'sulfur-dioxide':ti,ab OR 'sulfur-dioxide'/exp OR 'surfactant'/exp OR 'surfactant*':ti,ab OR 'TCDD':ti,ab OR 'teratogen*':ti,ab OR 'teratogenic':ti,ab OR 'teratogenic-agent'/exp OR 'teratogenicity'/exp OR 'tetrachlorodibenzodioxin':ti,ab OR 'tetrachloroethylene':ti,ab OR 'tetrachloroethylene'/exp OR 'Tin':ti,ab OR 'Tin'/exp OR 'tobacco smoke'/exp OR 'toluene':ti,ab OR 'toluene'/exp OR 'toxicant*':ti,ab OR 'toxin'/exp OR 'toxin*':ti,ab OR 'tributyltin':ti,ab OR 'tributyltin'/exp OR 'trichloroethane'/exp OR 'trichloroethane*':ti,ab OR 'trichloroethylene':ti,ab OR 'trichloroethylene'/exp OR 'ultrafine particle'/exp OR 'Vanadium':ti,ab OR 'Vanadium'/exp OR 'vinclozolin':ti,ab OR 'vinclozolin'/exp OR 'vinyl-chloride':ti,ab OR 'vinyl-chloride'/exp OR 'volatile-organic-compound'/exp OR 'volatile-organic-compound*':ti,ab OR 'warfarin':ti,ab OR 'warfarin'/exp OR 'water-pollutant'/exp OR 'water-pollutant*':ti,ab OR 'water-pollution':ti,ab OR 'water-pollution'/exp OR 'woodsmoke':ti,ab OR 'woodstove*':ti,ab OR 'xenobiotic agemt'/exp OR 'xenobiotic*':ti,ab OR 'xenoestrogen'/exp OR 'xenoestrogen*':ti,ab OR 'x-ray*':ti,ab OR 'xylene':ti,ab OR 'xylene'/exp)</p>
PubMed/MEDLINE	<p>((arteries[tiab] OR artery[tiab] OR arterial[tiab] OR carotid[tiab] OR coronary[tiab] OR heart[tiab] OR peripheral[tiab] OR renal[tiab] OR stenosis[tiab]) AND plaque*[tiab]) OR Arteriosclerosis[Mesh:NoExp] OR Atherogenesis[tiab] OR atheroma*[tiab] OR Atheroscleroses[tiab] OR Atherosclerosis[mh] OR Atherosclerosis[tiab] OR Atherosclerotic-plaque*[tiab] OR fatty-streak*[tiab] OR fibroatheroma*[tiab] OR foam-</p>

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	<p>cell*[tiab] OR Peripheral-Arterial-Disease*[tiab] OR Peripheral-Artery-Disease*[tiab] OR plaque,-atherosclerotic[mh] OR proatherogen*[tiab] OR pro-atherogen*[tiab])</p> <p>AND</p> <p>(abscess[tiab] OR acute-phase-reaction[tiab] OR acute-phase-response[tiab] OR Acute-phase-state[tiab] OR cellulitis[tiab] OR Empyema[tiab] OR Sepsis-syndrome[tiab] OR Sepsis-syndromes[tiab] OR Serositis[tiab] OR Suppuration[tiab] OR Systemic-Inflammatory-Response-Syndrome[tiab] OR anti-inflammat*[tiab] OR inflamed[tiab] OR Inflammat*[tiab] OR Inflammation[mh] OR inflammation-mediators[mh] OR proinflammat*[tiab] OR pro-inflammat*[tiab])</p> <p>AND</p> <p>(B-Cell-Differentiation-Factor[tiab] OR B-Cell-Stimulatory-Factor-2[tiab] OR BSF-2[tiab] OR Coagulation-Factor-I[tiab] OR C-reactive-Protein[mh] OR C-reactive-Protein[tiab] OR CRP[tiab] OR Factor-I[tiab] OR Fibrinogen[mh] OR Fibrinogen[tiab] OR Hepatocyte-Stimulating-Factor[tiab] OR Hybridoma-Growth-Factor[tiab] OR IFN-beta-2[tiab] OR IL6[tiab] OR IL-6[tiab] OR Interferon-beta-2[tiab] OR Interleukin-6[mh] OR Interleukin-6[tiab] OR MGI-2[tiab] OR Myeloid-Differentiation-Inducing-Protein[tiab] OR Plasmacytoma-Growth-Factor[tiab])</p> <p>AND</p> <p>("1,3-butadiene"[tiab] OR "2,3,7,8-tetrachlorodibenzo-p-dioxin"[tiab] OR "2-bromopropane"[tiab] OR "2-propanol"[tiab] OR "3,4-benzopyrene"[tiab] OR "benzo(a)pyrene"[mh] OR "benzo(a)pyrene"[tiab] OR "benzo-a-pyrene"[tiab] OR "Bisphenol-A"[tiab] OR "N,N-diethyltoluamide"[tiab] OR "PM(10)"[tiab] OR "PM(2.5)"[tiab] OR "PM10"[tiab] OR "PM2.5"[tiab] OR ((air[tiab] OR airborne[tiab] OR coarse[tiab] OR ultrafine[tiab] OR fine[tiab]) AND (particle*[tiab] OR particulate*[tiab])) OR ((air[tiab] OR outdoor[tiab] OR outdoors[tiab] OR outside[tiab] OR ambient[tiab] OR pollut*[tiab] OR emissions[tiab] OR exhaust*[tiab]) AND (sulfur-dioxide[mh] OR sulfur-dioxide[tiab] OR SO2[tiab] OR ozone[mh] OR ozone[tiab] OR O3[tiab] OR hydrogen-sulfide[mh] OR hydrogen-sulfide[tiab] OR H2S[tiab] OR carbon-monoxide[mh] OR carbon-monoxide[tiab] OR nitric-oxide[tiab] OR nitrogen-oxide[tiab] OR nitrogen-oxides[tiab] OR nitrogen-dioxide[mh] OR nitrogen-dioxide[tiab] OR NOx[tiab] OR "NO(x)"[tiab] OR NO2[tiab])) OR ((fire[tiab] OR flame[tiab]) AND retardant*[tiab]) OR ((halogenated[tiab] OR chlorinated[tiab] OR brominated[tiab] OR polybrominated[tiab]) AND diphenyl-ethers[tiab]) OR ((metal[tiab] OR metals[tiab]) AND lead[tiab]) OR ((occupation[tiab] OR occupational[tiab] OR occupations[tiab] OR workplace[tiab] OR work-place[tiab] OR work-related[tiab] OR worker[tiab] OR workers[tiab] OR employee[tiab] OR employees[tiab]) AND (exposure[tiab] OR exposed[tiab] OR chemical[tiab] OR chemicals[tiab] OR hazards[tiab] OR hazard[tiab])) OR ((smoke[tiab] OR smoking[tiab]) AND (cigarette[tiab] OR cigarettes[tiab] OR tobacco[tiab] OR cigar[tiab] OR cigars[tiab])) OR ((vehicle[tiab] OR vehicles[tiab] OR vehicular[tiab] OR auto[tiab] OR automobile[tiab] OR automobiles[tiab] OR autos[tiab] OR bus[tiab] OR buses[tiab] OR car[tiab] OR truck[tiab] OR trucks[tiab] OR engine[tiab] OR cars[tiab] OR traffic[tiab] OR transport*[tiab]) AND (emissions[tiab] OR exhaust[tiab] OR fume[tiab] OR fumes[tiab])) OR ((wood[mh] OR wood[tiab] OR</p>

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	<p>firewood[tiab] OR biomass[tiab] OR charcoal[tiab] OR fuel[tiab] OR fuels[tiab] OR gas[tiab] OR gasoline[tiab] OR kerosene[tiab] OR dung[tiab] OR manure[tiab]) AND (smoke[mh] OR smoke[tiab] OR smoking[tiab] OR combust[tiab] OR combusted[tiab] OR combustible[tiab] OR combustibles[tiab] OR burned[tiab] OR burn[tiab] OR burning[tiab])) OR (endocrine[tiab] AND (disrupt[tiab] OR disruptor[tiab] OR disruptors[tiab])) OR (environment*[ti] AND epigen*[ti]) OR (indoor[tiab] AND (air[tiab] OR environment[tiab] OR exposure[tiab] OR pollution[tiab] OR Smoke[tiab])) OR acetone[tiab] OR agent-orange[tiab] OR agrochemical*[tiab] OR air-pollutant[tiab] OR air-pollutants[mh] OR air-pollutants[pa] OR air-pollutants[tiab] OR air-pollution[mh] OR air-pollution[tiab] OR air-quality[tiab] OR aldrin[tiab] OR allergen*[tiab] OR Allergens[mh] OR Amitraz[tiab] OR aromatic-hydrocarbons[tiab] OR arsenate*[tiab] OR arsenic[mh] OR arsenic[tiab] OR arsenical*[tiab] OR arsenicals[mh] OR arsenite*[tiab] OR atrazine[tiab] OR avermectin[tiab] OR benzene[mh] OR benzene[tiab] OR benzopyrene[tiab] OR black-carbon[tiab] OR butyl-benzyl-phthalate[tiab] OR butyl-phthalate[tiab] OR cadmium[tiab] OR captan[tiab] OR carbaryl[tiab] OR carbofuran[tiab] OR carbon-black[tiab] OR carbon-monoxide[mh] OR carbon-monoxide[tiab] OR carcinogen[tiab] OR carcinogenic[tiab] OR carcinogens[mh] OR carcinogens[tiab] OR cardiotox*[tiab] OR cardiotoxins[mh] OR Chemical-compound*[tiab] OR chemical-exposure*[tiab] OR chemically-induced[sh] OR chemical-mixture*[tiab] OR chemical-product*[tiab] OR chemical-substance*[tiab] OR chlordan[tiab] OR chlorfenvinphos[tiab] OR chlorinated-hydrocarbons[tiab] OR chlorobenzene*[tiab] OR chlorofluorocarbon*[tiab] OR chlorpyrifos[tiab] OR chromium[tiab] OR cobalt[tiab] OR cooker*[tiab] OR cooking[mh] OR cooking[tiab] OR cookstove*[tiab] OR cook-stove*[tiab] OR coumaphos[tiab] OR cytotoxins[mh] OR cytotox*[tiab] OR DDT[tiab] OR deet[tiab] OR dermatox*[tiab] OR dermatoxins[mh] OR diazinon[tiab] OR Dibutyl-Phthalate[mh] OR dibutyl-phthalate[tiab] OR dichlorodiphenyltrichloroethane*[tiab] OR dichlorophenyl-dichloroethylene[tiab] OR dichlorvos[tiab] OR dieldrin[tiab] OR diesel[tiab] OR Diethylstilbestrol[mh] OR diethylstilbestrol[tiab] OR dimethyl-phthalate[tiab] OR dioxane*[tiab] OR dioxin*[tiab] OR dioxins[mh] OR dust[mh] OR dust[tiab] OR elemental-carbon[tiab] OR Endocrine-disrupt*[tiab] OR Endocrine-disruptors[mh] OR endosulfan[tiab] OR endrin[tiab] OR Environment[mh:noexp] OR Environmental-agent*[tiab] OR environmental-chemical*[tiab] OR environmental-compound*[tiab] OR environmental-contaminant*[tiab] OR environmental-determinant*[tiab] OR environmental-epigenetic*[tiab] OR environmental-estrogen*[tiab] OR environmental-exposure[mh] OR environmental-exposure*[tiab] OR environmental-factor*[tiab] OR environmental-influence*[tiab] OR environmental-pollutant*[tiab] OR environmental-pollutants[mh:noexp] OR environmental-pollutants[pa] OR environmental-pollution[mh:noexp] OR environmental-pollution[tiab] OR environmental-stress*[tiab] OR fireplace*[tiab] OR Flame-retardant*[tiab] OR Flame-retardants[mh] OR flame-retardants[pa] OR Formaldehyde[mh] OR formaldehyde[tiab] OR fossil-fuel*[tiab] OR fossil-fuels[mh] OR fungicide*[tiab] OR gasoline*[tiab] OR halogenated-diphenyl-ethers[mh] OR hazardous-compound*[tiab] OR hazardous-exposure*[tiab] OR hazardous-mixture*[tiab] OR hazardous-product*[tiab] OR hazardous-substance*[tiab] OR hazardous-substances[mh] OR hazardous-substances[pa] OR heater*[tiab] OR heating[mh] OR heating[tiab] OR heavy-metal[tiab] OR heavy-metals[tiab] OR heptachlor[tiab] OR herbicide*[tiab] OR hydrocarbons,-aromatic[mh:noexp] OR Hydrocarbons-chlorinated[mh] OR hydrogen-sulfide[mh] OR hydrogen-sulfide[tiab] OR immunotox*[tiab] OR immunotoxins[mh] OR indoors[tiab] OR industrial-chemical*[tiab] OR industrial-compound*[tiab] OR insecticide*[tiab] OR irradiated[tiab] OR lead-poisoning[mh] OR linalool[tiab] OR malathion[tiab] OR Mercury[tiab] OR metals[tiab] OR</p>

Evidence Map: Literature Search Strategy	
Database	Search Terms
	<p>Metals,-heavy[mh] OR methoxychlor[tiab] OR Methylmercury[tiab] OR methylmercury-compounds[mh] OR mold[tiab] OR motor-vehicle*[tiab] OR motor-vehicles[mh] OR mutagen[tiab] OR mutagenic[tiab] OR mutagens[mh] OR mutagens[tiab] OR nephrotox*[tiab] OR neurotox*[tiab] OR neurotoxins[mh] OR Nickel[tiab] OR nitrate*[tiab] OR nitrates[mh] OR nitrogen-dioxide[mh] OR nitrogen-dioxide[tiab] OR noxae[mh:noexp] OR noxae[tiab] OR Occupational-exposure[mh] OR organic-chlorine[tiab] OR organic-solvent[tiab] OR organochlorin*[tiab] OR organophosphorus*[tiab] OR Organotin[mh] OR organotin*[tiab] OR oven*[tiab] OR ozone[mh] OR ozone[tiab] OR PAHs[tiab] OR paraben*[tiab] OR paraquat[tiab] OR parathion[tiab] OR particulate-matter[mh] OR particulate-matter[tiab] OR passive-smoke[tiab] OR passive-smoking[tiab] OR PBDE*[tiab] OR PCBs[tiab] OR PCDE*[tiab] OR pentachlorophenol[tiab] OR perchlorate*[tiab] OR perfluorinat*[tiab] OR permethrin[tiab] OR persistent-organic-pollutant*[tiab] OR Pesticid*[tiab] OR Pesticides[mh] OR pesticides[pa] OR petrol*[tiab] OR phthalate*[tiab] OR phytoestrogen*[tiab] OR plasticizer*[tiab] OR Plasticizers[mh] OR plasticizers[pa] OR pollen[tiab] OR pollutant*[tiab] OR pollution[tiab] OR polychlorinated-biphenyl[tiab] OR polychlorinated-biphenyls[tiab] OR polychlorobiphenyl[tiab] OR polycyclic-aromatic-hydrocarbons[tiab] OR Polycyclic-hydrocarbons,-aromatic[mh:noexp] OR pyrethrin*[tiab] OR radiation[tiab] OR radon[mh] OR radon[tiab] OR repellent*[tiab] OR rodenticide*[tiab] OR rotenone[tiab] OR secondhand-smoke[tiab] OR second-hand-smoke[tiab] OR secondhand-smoking[tiab] OR second-hand-smoking[tiab] OR smog[mh] OR smog[tiab] OR smoking[mh] OR solvent*[tiab] OR Solvents[mh] OR soot[mh] OR soot[tiab] OR Specialty-Uses-of-Chemicals[mh] OR spores[tiab] OR stilbene-estrogen[tiab] OR stilbestrol[tiab] OR stove*[tiab] OR sulfur-dioxide[mh] OR sulfur-dioxide[tiab] OR surfactant*[tiab] OR TCDD[tiab] OR teratogen*[tiab] OR teratogenic[tiab] OR teratogens[mh] OR tetrachlorodibenzodioxin[tiab] OR tetrachloroethylene[tiab] OR Tin[tiab] OR tobacco-smoke-pollution[mh] OR toluene[tiab] OR Toxic-Actions[mh] OR toxicant*[tiab] OR toxicity[sh] OR toxin*[tiab] OR tributyltin[tiab] OR trichloroethane*[tiab] OR trichloroethylene[tiab] OR Vanadium[tiab] OR vehicle-emissions[mh] OR vinclozolin[tiab] OR vinyl-chloride[tiab] OR volatile-organic-compound*[tiab] OR volatile-organic-compounds[mh] OR warfarin[tiab] OR water-pollutant*[tiab] OR water-pollutants[mh] OR water-pollution[mh] OR water-pollution[tiab] OR woodsmoke[tiab] OR woodstove*[tiab] OR xenobiotic*[tiab] OR xenoestrogen*[tiab] OR x-ray*[tiab] OR x-rays[mh] OR xylene[tiab] OR xylenes[mh])</p>
Scopus	Identical to Web of Science terms; searched in title/abstract only.
Toxline	<p>Note: Toxline search only includes atherosclerosis, inflammation, and biomarker terms</p> <p>((artery OR renal heart OR angina OR arrhythmia OR arrhythmias) AND plaque) OR Arteriosclerosis OR ((arterial OR carotid OR coronary) AND plaque) OR Atherogenesis OR atheroma OR atheromas OR Atherosclerosis OR Atherosclerosis OR Atherosclerotic OR fatty-streak OR fatty-streaks OR fibroatheroma OR fibroatheromas OR foam-cell OR foam-cells OR Peripheral-Arterial-Disease OR Peripheral-Arterial-Diseases OR Peripheral-Artery-Disease OR Peripheral-Artery-Diseases OR proatherogen* OR pro-atherogen*)</p> <p>AND</p> <p>(abscess OR acute-phase-reaction OR acute-phase-response OR Acute-phase-state OR cellulitis OR Empyema OR Sepsis-syndrome OR Sepsis-syndromes OR Serositis OR Suppuration OR Systemic-Inflammatory-Response-Syndrome OR anti-inflammation OR</p>

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	<p>anti-inflammatory OR inflamed OR Inflammation OR inflammatory OR proinflammatory OR proinflammation OR pro-inflammatory OR pro-inflammation)</p> <p>AND</p> <p>(B-Cell-Differentiation-Factor OR B-Cell-Stimulatory-Factor-2 OR BSF-2 OR Coagulation-Factor-I OR C-reactive-Protein OR CRP OR Factor-I OR Fibrinogen OR Hepatocyte-Stimulating-Factor OR Hybridoma-Growth-Factor OR IFN-beta-2 OR IL6 OR IL-6 OR Interferon-beta-2 OR Interleukin-6 OR MGI-2 OR Myeloid-Differentiation-Inducing-Protein OR Plasmacytoma-Growth-Factor)</p>
Web of Science	<p>((arteries OR artery OR arterial OR carotid OR coronary OR heart OR peripheral OR renal OR stenosis) AND plaque*) OR Atherogenesis OR atheroma* OR Atheroscleroses OR Atherosclerosis OR Atherosclerotic-plaque* OR fatty-streak* OR fibroatheroma* OR foam-cell* OR Peripheral-Arterial-Disease* OR Peripheral-Artery-Disease* OR proatherogen* OR pro-atherogen*)</p> <p>AND</p> <p>(abscess OR acute-phase-reaction OR acute-phase-response OR Acute-phase-state OR cellulitis OR Empyema OR Sepsis-syndrome OR Sepsis-syndromes OR Serositis OR Suppuration OR Systemic-Inflammatory-Response-Syndrome OR anti-inflamat* OR inflamed OR Inflamat* OR proinflamat* OR pro-inflamat*)</p> <p>(B-Cell-Differentiation-Factor OR B-Cell-Stimulatory-Factor-2 OR BSF-2 OR Coagulation-Factor-I OR C-reactive-Protein OR CRP OR Factor-I OR Fibrinogen OR Hepatocyte-Stimulating-Factor OR Hybridoma-Growth-Factor OR IFN-beta-2 OR IL6 OR IL-6 OR Interferon-beta-2 OR Interleukin-6 OR MGI-2 OR Myeloid-Differentiation-Inducing-Protein OR Plasmacytoma-Growth-Factor)</p> <p>AND ("1,3-butadiene" OR "2,3,7,8-tetrachlorodibenzo-p-dioxin" OR "2-bromopropane" OR "2-propanol" OR "3,4-benzopyrene" OR "benzo(a)pyrene" OR "benzo-a-pyrene" OR "Bisphenol-A" OR "N,N-diethyltoluamide" OR "PM(10)" OR "PM(2.5)" OR "PM10" OR "PM2.5" OR ((air OR airborne OR coarse OR ultrafine OR fine) AND (particle* OR particulate*)) OR ((air OR outdoor OR outdoors OR outside OR ambient OR pollut* OR emissions OR exhaust*) AND (sulfur-dioxide OR sulfur-dioxide OR SO2 OR ozone OR ozone OR O3 OR hydrogen-sulfide OR hydrogen-sulfide OR H2S OR carbon-monoxide OR carbon-monoxide OR nitric-oxide OR nitrogen-oxide OR nitrogen-oxides OR nitrogen-dioxide OR nitrogen-dioxide OR NOx OR "NO(x)" OR NO2)) OR ((fire OR flame) AND retardant*) OR ((halogenated OR chlorinated OR brominated OR polybrominated) AND diphenyl-ethers) OR ((metal OR metals) AND lead) OR ((occupation OR occupational OR occupations OR workplace OR work-place OR work-related OR worker OR workers OR employee OR employees) AND (exposure OR exposed OR chemical OR chemicals OR hazards OR hazard)) OR ((smoke OR smoking) AND (cigarette OR cigarettes OR tobacco OR cigar OR cigars)) OR ((vehicle OR vehicles OR vehicular OR auto OR automobile OR automobiles OR autos OR bus OR buses OR car OR truck OR trucks OR engine OR cars OR traffic OR transport*) AND (emissions OR exhaust OR fume OR fumes)) OR ((wood OR wood OR firewood OR biomass OR charcoal OR fuel OR fuels OR gas OR gasoline OR kerosene OR dung OR manure) AND (smoke OR smoke OR smoking OR combust OR combusted OR</p>

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	<p>combustible OR combustibles OR burned OR burn OR burning)) OR (endocrine AND (disrupt OR disruptor OR disruptors)) OR (environment* AND epigen*) OR (indoor AND (air OR environment OR exposure OR pollution OR Smoke)) OR acetone OR agent-orange OR agrochemical* OR air-pollutant OR air-pollutants OR air-pollution OR air-quality OR aldrin OR allergen* OR Amitraz OR aromatic-hydrocarbons OR arsenate* OR arsenic OR arsenical* OR arsenite* OR atrazine OR avermectin OR benzene OR benzopyrene OR black-carbon OR butyl-benzyl-phthalate OR butyl-phthalate OR cadmium OR captan OR carbaryl OR carbofuran OR carbon-black OR carbon-monoxide OR carcinogen OR carcinogenic OR carcinogens OR cardiotox* OR Chemical-compound* OR chemical-exposure* OR chemical-mixture* OR chemical-product* OR chemical-substance* OR chlordan OR chlorfenvinphos OR chlorinated-hydrocarbons OR chlorobenzene* OR chlorofluorocarbon* OR chlorpyrifos OR chromium OR cobalt OR cooker* OR cooking OR cookstove* OR cook-stove* OR coumaphos OR cytotox* OR DDT OR deet OR dermatox* OR diazinon OR dibutyl-phthalate OR dichlorodiphenyltrichloroethane* OR dichlorophenyl-dichloroethylene OR dichlorvos OR dieldrin OR diesel OR diethylstilbestrol OR dimethyl-phthalate OR dioxane* OR dioxin* OR dust OR elemental-carbon OR Endocrine-disrupt* OR endosulfan OR endrin OR Environmental-agent* OR environmental-chemical* OR environmental-compound* OR environmental-contaminant* OR environmental-determinant* OR environmental-epigenetic* OR environmental-estrogen* OR environmental-exposure* OR environmental-factor* OR environmental-influence* OR environmental-pollutant* OR environmental-pollution OR environmental-stress* OR fireplace* OR Flame-retardant* OR formaldehyde OR fossil-fuel* OR fungicide* OR gasoline* OR hazardous-compound* OR hazardous-exposure* OR hazardous-mixture* OR hazardous-product* OR hazardous-substance* OR heater* OR heating OR heavy-metal OR heavy-metals OR heptachlor OR herbicide* OR hydrogen-sulfide OR immunotox* OR indoors OR industrial-chemical* OR industrial-compound* OR insecticide* OR irradiated OR linalool OR malathion OR Mercury OR metals OR methoxychlor OR Methylmercury OR mold OR motor-vehicle* OR mutagen OR mutagenic OR mutagens OR nephrotox* OR neurotox* OR Nickel OR nitrate* OR nitrogen-dioxide OR noxae OR organic-chlorine OR organic-solvent OR organochlorin* OR organophosphorus* OR organotin* OR oven* OR ozone OR PAHs OR paraben* OR paraquat OR parathion OR particulate-matter OR passive-smoke OR passive-smoking OR PBDE* OR PCBs OR PCDE* OR pentachlorophenol OR perchlorate* OR perfluorinat* OR permethrin OR persistent-organic-pollutant* OR Pesticid* OR petrol* OR phthalate* OR phytoestrogen* OR plasticizer* OR pollen OR pollutant* OR pollution OR polychlorinated-biphenyl OR polychlorinated-biphenyls OR polychlorobiphenyl OR polycyclic-aromatic-hydrocarbons OR pyrethrin* OR radiation OR radon OR repellent* OR rodenticide* OR rotenone OR secondhand-smoke OR second-hand-smoke OR secondhand-smoking OR second-hand-smoking OR smog OR solvent* OR soot OR spores OR stilbene-estrogen OR stilbestrol OR stove* OR sulfur-dioxide OR surfactant* OR TCDD OR teratogen* OR teratogenic OR tetrachlorodibenzodioxin OR tetrachloroethylene OR Tin OR toluene OR toxicant* OR toxin* OR tributyltin OR trichloroethane* OR trichloroethylene OR Vanadium OR vinclozolin OR vinyl-chloride OR volatile-organic-compound* OR warfarin OR water-pollutant* OR water-pollution OR woodsmoke OR woodstove* OR xenobiotic* OR xenoestrogen* OR x-ray* OR xylene)</p>