Supplemental information

**Table S1**. Tittle, author and year of the 52 reviews analyzed in this study that reviewed the relationship between heavy metals and human male fertility.

| Reference | Tittle |
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| **Abarikwu 2013** | Causes and risk factors for male-factor infertility in Nigeria |
| **Ashiru and Odusanya 2009** | Fertility and occupational hazards: Review of the literature |
| **Balabanic and Klemencic 2014** | Diet containing endocrine-disruptors and reproductive health |
| **Bjørklund et al. 2019** | Mercury exposure and its effects on fertility and pregnancy outcome |
| **Bonde 2010** | Male reproductive organs are at risk from environmental hazards |
| **Dai et al. 2015** | The hazardous effects of tobacco smoking on male fertility |
| **de Angelis et al. 2017** | The environment and male reproduction: The effect of cadmium exposure on reproductive function and its implication in fertility |
| **DeCelis et al. 1996** | Toxicology of male reproduction in animals and humans |
| **Droller 1996** | Environment and the genitourinary tract |
| **Fallah et al. 2018** | Zinc is an essential element for male fertility: A review of zn roles in men's health, germination, sperm quality, and fertilization |
| **Figa-Talamanca et al. 2001** | Occupational exposures to metals, solvents and pesticides: Recent evidence on male reproductive effects and biological markers. |
| **Giudice 2006** | Infertility and the environment: The medical context |
| **Grigore and Indrei, 2001** | The role of heat shock proteins in reproduction |
| **Hales and Robaire 2001** | Review - paternal exposure to drugs and environmental chemicals: Effects on progeny outcome |
| **Henriques et al. 2019** | Exposure to mercury and human reproductive health: A systematic review |
| **Hruska et al. 2000** | Environmental factors in infertility |
| **Ilieva et al. 2020** | Toxic effects of heavy metals (lead and cadmium) on sperm quality and male fertility |
| **Jenardhanana et a.l 2016** | Effect of environmental contaminants on spermatogenesis. |
| **Jensen et al. 2006** | The influence of occupational exposure on male reproductive function |
| **Kaminski et al. 2020** | External and genetic conditions determining male infertility |
| **Kumar 2004** | Occupational exposure associated with reproductive dysfunction |
| **Kumar 2018** | Occupational and environmental exposure to lead and reproductive health impairment: An overview |

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| **Kumar and Sharma 2019** | Cadmium toxicity: Effects on human reproduction and fertility |
| **Lavranos et al. 2012** | Investigating ROS sources in male infertility: A common end for numerous pathways |
| **Lovakovic 2020** | Cadmium, arsenic, and lead: Elements affecting male reproductive health |
| **Ma et al. 2016** | Effects of environmental contaminants on fertility and reproductive health. |
| **Manfo et al. 2014** | Effect of environmental contaminants on mammalian testis. |
| **Martynowicz et al. 2005** | Effects of cadmium on testis function. |
| **Marzec-Wroblewska et al. 2012** | Influence of chemical elements on mammalian spermatozoa |
| **Najafi et al. 2015** | Air pollution and quality of sperm: A meta-analysis. |
| **Neuer et al. 2000** | The role of heat shock proteins in reproduction |
| **Ogorek et al. 2017** | Role of copper in the process of spermatogenesis |
| **Pieczynska and Grajeta 2015** | The role of selenium in human conception and pregnancy |
| **Plunk and Richards 2020** | Endocrine-disrupting air pollutants and their effects on the hypothalamus-pituitary-gonadal axis |
| **Ramos-Trevino et al. 2018** | Toxic effect of cadmium, lead, and arsenic on the Sertoli cell: Mechanisms of damage involved. |
| **Reis et al. 2015** | Sertoli cell as a model in male reproductive toxicology: Advantages and disadvantages |
| **Rezk and Sikka 2011** | Developmental and reproductive disorders: Role of endocrine disruptors in testicular toxicity |
| **Rier 2008** | Environmental immune disruption: A comorbidity factor for reproduction? |
| **Rogers 2008** | Tobacco and pregnancy: Overview of exposures and effects |
| **Sengupta et al. 2017** | Evidence for decreasing sperm count in African population from 1965 to 2015 |
| **Sheiner et al. 2003** | Effect of occupational exposures on male fertility: Literature review |
| **Sheweita et al. 2005** | Mechanisms of male infertility: Role of antioxidants |
| **Siu et al. 2009** | Cadmium-induced testicular injury |
| **Skolarczyk et al. 2018** | The impact of cadmium on male infertility |
| **Takeda et al. 2004** | Endocrine-disrupting activity of chemicals in diesel exhaust and diesel exhaust particles |
| **Thompson and Bannigan, 2008** | Cadmium: Toxic effects on the reproductive system and the embryo |
| **Vigeh et al. 2011** | How does lead induce male infertility? |
| **Wan et al. 2013** | Targeting testis-specific proteins to inhibit spermatogenesis: Lesson from endocrine disrupting chemicals. |
| **Webb et al. 2014** | Developmental and reproductive effects of chemicals associated with unconventional oil and natural gas operations |

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| **Wirth and Mijal, 2010** | Adverse effects of low-level heavy metal exposure on male reproductive function |
| **Zenzes 2000** | Smoking and reproduction: Gene damage to human gametes and embryos |
| **Zhang et al. 2019** | Relationship between cadmium content in semen and male infertility: A meta-analysis |

**Table S2**. Tittle, author and year of 2 clinical trials analyzed in this study that studied the relationship between heavy metals and human male fertility.

| Author | Tittle |
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| **Alexander et al. 1998** | Interaction of blood lead and delta-aminolevulinic acid dehydratase genotype on markers of heme synthesis and sperm production in lead smelter workers |
| **Ali et al. 2017** | Mapping fifteen trace elements in human seminal plasma and sperm DNA |

**Table S3**. Tittle, author and year of the 90 articles analyzed in this study that studied the relationship between heavy metals and human male fertility.

| Author | Tittle |
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| **Apostoli et al. 1999** | Critical aspects of male fertility in the assessment of exposure to lead |
| **Araya et al. 2003** | Human spermatozoa motility analysis in a ringer's solution containing cupric ions |
| **Balabanic et al. 2011** | Negative impact of endocrine-disrupting compounds on human reproductive health |
| **Benoff et al. 2000** | Metal ions and human sperm mannose receptors |
| **Bloom et al. 2015** | Birth outcomes and background exposures to select elements, the longitudinal investigation of fertility and the environment (LIFE) |
| **Chen et al. 2015** | Rare earths exposure and male infertility: The injury mechanism study of rare earths on male mice and human sperm. |
| **Comhaire et al. 2007** | Sperm quality, birth rates and the environment in Flanders (Belgium) |
| **Dandevi et al. 2003** | Semen quality of Indian welders occupationally exposed to nickel and chromium |

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| **De Fleurian et al. 2009** | Occupational exposures obtained by questionnaire in clinical practice and their association with semen quality |
| **Dickman and Leung 1998** | Mercury and organochlorine exposure from fish consumption in Hong Kong. |
| **Dickman et al. 1998** | Hong Kong male subfertility links to mercury in human hair and fish. |
| **Elsamanoudy et al. 2014** | Possible effects of metallosis on spermatozoal apoptotic genes expression in individuals with intramedullary nailing prosthesis |
| **Evans 2011** | Endocrine disruptors |
| **Fatima et al. 2015** | Association of blood and semen lead and zinc level with semen parameter in the male partner of infertile couple |
| **Garcia-Herrero et al. 2011** | Differential transcriptomic profile in spermatozoa achieving pregnancy or not via ICSI |
| **Gerhard et al. 1998** | Heavy metals and fertility |
| **Ghaffari and Motlagh 2011** | In vitro effect of lead, silver, tin, mercury, indium and bismuth on human sperm creatine kinase activity: A presumable mechanism for men infertility |
| **Ghiasvand et al. 2020** | The association between animal flesh foods consumption and semen parameters among infertile Iranian men: A cross-sectional study |
| **Hanf et al. 1996** | Mercury in urine and ejaculate in husbands of barren couples |
| **Hardneck et al. 2018** | Quantitative assessment of heavy metal effects on sperm function using computer-aided sperm analysis and cytotoxicity assays. |
| **Hassan et al. 2019** | The protective effect of epigallocatechin-3-gallate on testicular oxidative stress in lead-induced toxicity mediated by Cyp19 gene / estradiol level |
| **He et al. 2016** | Lead inhibits human sperm functions by reducing the levels of intracellular calcium, cAMP, and tyrosine phosphorylation |
| **He et al. 2020** | Heavy metal exposure, oxidative stress and semen quality: Exploring associations and mediation effects in reproductive-aged men |
| **Huang et al. 2001** | In vitro effects of metal ions (Fe2+, Mn2+, Pb2+) on sperm motility and lipid peroxidation in human semen |
| **Hunter 2011** | The cost of living longer fertility trades with immunity and life expectancy |
| **Inhorn et al. 2008** | Occupational and environmental exposures to heavy metals: Risk factors for male infertility in Lebanon? |
| **Irgens et al. 1999** | The effect of male occupational exposure in infertile couples in Norway. |
| **Jeng et al. 2015** | Role of low exposure to metals as male reproductive toxicants. |
| **Kahraman et al. 2012** | The effect of blood and seminal plasma heavy metal and trace element levels on sperm quality |
| **Keck et al. 1995** | Lack of correlation between cadmium in seminal plasma and fertility status of nonexposed individuals and 2 cadmium-exposed patients |
| **Kim et al. 2014** | Toxic metals in seminal plasma and in vitro fertilization (IVF) outcomes |
| **Kislitskaya et al. 2015** | Disturbance of antioxidant enzymes and purine metabolism in the ejaculate of men living in disadvantaged areas of Kyzylorda region. |
| **Kumar et al. 2000** | Chlorinated pesticides and heavy metals in human semen |

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| **Kumar et al. 2018** | Role of environmental factors & oxidative stress with respect to in vitro fertilization outcome |
| **Kuo et al. 1997** | Semen quality in workers with long-term lead exposure: A preliminary study in Taiwan |
| **Leite et al. 2015** | Environmentally realistic doses of cadmium as a possible etiologic agent for idiopathic pathologies |
| **Lettieri et al. 2020** | Discovery of the involvement in DNA oxidative damage of human sperm nuclear basic proteins of healthy young men living in polluted areas |
| **Lettieriet al. 2020** | Molecular alterations in spermatozoa of a family case living in the land of fires-A first look at possible transgenerational effects of pollutants |
| **Li et al. 2008** | Are serum zinc and copper levels related to semen quality? |
| **Li et al. 2015** | Biomonitoring of blood heavy metals and reproductive hormone level related to low semen quality |
| **Li et al. 2014** | Cadmium, chromium, and copper concentration plus semen-quality in environmental pollution site, china |
| **Li et al. 2012** | Effects of manganese on routine semen quality parameters: Results from a population-based study in china |
| **Li et al. 2016** | Association between environmental exposure to cadmium and human semen quality. |
| **Lin et al. 1996** | Fertility rates among lead workers and professional bus drivers: A comparative study |
| **Louis et al. 2012** | Heavy metals and couple fecundity, the LIFE study |
| **Marchiani et al. 2019** | Acute effects on human sperm exposed in vitro to cadmium chloride and diisobutyl phthalate. |
| **Mendiola et al. 2011** | Relationships between heavy metal concentrations in three different body fluids and male reproductive parameters: A pilot study |
| **Minguez-Alarcon et al. 2018** | Hair mercury (hg) levels, fish consumption and semen parameters among men attending a fertility center. |
| **Mitra et al. 2020** | Lead and cadmium exposure induces male reproductive dysfunction by modulating the expression profiles of apoptotic and survival signal proteins in tea -garden workers |
| **Monsees et al. 2000** | Sertoli cells as a target for reproductive hazards |
| **Moran-Martinez et al. 2013** | Chronic environmental exposure to lead affects semen quality in a Mexican men population |
| **Mukhopadhyay et al. 2010** | CASA-based sperm kinematics of environmental risk factor-exposed human semen samples designated as normozoospermic in conventional analysis |
| **Murado et al. 2014** | Oversimplification and overstandardization in biological methods: Sperm bioassays in ecotoxicology as a case of study and a proposal for their reformulation. |
| **Naha and Chowdhury 2006** | Inorganic lead exposure in battery and paint factory: Effect on human sperm structure and functional activity |
| **Naha et al. 2005** | Structural alteration of spermatozoa in the persons employed in lead acid battery factor |
| **Nath et al. 2010** | Heavy metal contaminants and male reproductive health |

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| **Nivsarkar et al. 1998** | A regulatory role of sulfhydryl groups in modulation of sperm membrane conformation by heavy metals: Sulfhydryl groups as markers for infertility assessment |
| **Nykolaichuk et al. 2020** | Impact of environmental factors on male reproductive health |
| **Pant et al.2013** | Semen quality of environmentally exposed human population: The toxicological consequence. |
| **Pant et al. 2003** | Lead and cadmium concentration in the seminal plasma of men in the general population: Correlation with sperm quality. |
| **Pavlova and Atanassova 2018** | Impact of cadmium on male fertility |
| **Petrelli et al. 2001** | Occupational exposure and male fertility. results of an Italian multicenter study in an exposed population]. |
| **Quansah and Jaakkola 2009** | Paternal and maternal exposure to welding fumes and metal dusts or fumes and adverse pregnancy outcomes |
| **Rao et al. 2015** | Evaluation of semen quality in 1808 university students, from Wuhan, central china |
| **Riaz et al. 2016** | Impact of reactive oxygen species on antioxidant capacity of male reproductive system. |
| **Robert et al. 1997** | Characterization of prostate-specific antigen proteolytic activity on its major physiological substrate, the sperm motility inhibitor precursor semenogelin I |
| **Sengupta et al. 2013** | Human sperm and other seminal constituents in male infertile patients from arsenic and cadmium rich areas of southern assam. |
| **Shi et al. 2020** | Interaction effect of polycyclic aromatic hydrocarbon metabolites and cadmium on semen quality in nonsmokers |
| **Skandhan et al. 2017** | Level of copper in human split ejaculate |
| **Slivkova et al. 2009** | Concentration of trace elements in human semen and relation to spermatozoa quality. |
| **Snijder et al. 2011** | Occupational exposure to endocrine disruptors and time to pregnancy among couples in a large birth cohort study: The generation R study |
| **Sobolev et al. 2018** | Biological role of selenium in the organism of animals and humans |
| **Stassen et al. 2012** | Metal exposure and reproductive disorders in indigenous communities living along the Pilcomayo river, Bolivia |
| **Stoltenberg et al. 1997** | Histochemical demonstration of zinc ions in human epididymis using autometallography. |
| **Stoltenberg et al. 1997** | Histochemical demonstration of zinc ions in ejaculated human semen |
| **Sukhn et al. 2018** | Associations of semen quality with non-essential heavy metals in blood and seminal fluid: Data from the environment and male infertility (EMI) study in Lebanon. |
| **Sun et al. 2017** | Heavy metal level in human semen with different fertility: A meta-analysis. |
| **Telisman et al. 2007** | Reproductive toxicity of low-level lead exposure in men. |
| **Telisman et al. 2000** | Semen quality and reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc, and copper in men |

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| **Wang et al. 2017** | Associations between urinary polycyclic aromatic hydrocarbon metabolites and serum testosterone in US adult males: National health and nutrition examination survey 2011-2012. |
| **Wang et al. 2016** | Variability of metal levels in spot, first morning, and 24-hour urine samples over a 3-month period in healthy adult Chinese men |
| **Wang et al. 2017** | Relationships between seminal plasma metals/metalloids and semen quality, sperm apoptosis and DNA integrity |
| **Wijesekara et al. 2015** | Environmental and occupational exposures as a cause of male infertility |
| **Wu et al. 2012** | Lead level in seminal plasma may affect semen quality for men without occupational exposure to lead |
| **Wu et al. 2020** | Associations of toxic and essential trace elements in serum, follicular fluid, and seminal plasma with in vitro fertilization outcomes |
| **Wulff et al. 1997** | Infertility in an industrial setting - A population-based study from northern Sweden. |
| **Yoshida et al. 2008** | Physiological roles of semenogelin I and zinc in sperm motility and semen coagulation on ejaculation in humans |
| **Zafar et al. 2015** | Toxic metals signature in the human seminal plasma of Pakistani population and their potential role in male infertility |
| **Zeng et al. 2015** | Urinary metal concentrations in relation to semen quality: A cross-sectional study in china |
| **Zhou et al. 2016** | Evaluation of urinary metal concentrations and sperm DNA damage in infertile men from an infertility clinic |