Assessing the Harm of the Illicit Tobacco Trade: A Systematic Review of Heavy Metal Contamination in Cigarettes and Their Health Implications

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Background of the Study

According to the study conducted by the World Health Organization in November 2023, tobacco use is responsible for the premature deaths of over 8 million individuals annually[1]. In the WHO report, most cases of premature deaths are caused by direct tobacco use. The evidence of harmful effects of tobacco inhalation on human health is steadily growing. Tobacco comprises an array of toxic constituents, of which at least 69 are carcinogenic. Some toxic substances included arsenic, cadmium, lead, nickel, chromium, and mercury. Smoking has been linked to a higher risk of cancer and respiratory diseases, among other harmful health effects. Moreover, smoking possesses the capacity to affect nearly every human organ, leading to the development of skin and mucosal lesions, cardiovascular diseases, infertility, miscarriage, and low birthweight.

In terms of reducing tobacco use and enhancing public health, tobacco taxation is among the most effective policies. In the Philippines, the Sin Tax Reform Act of 2012 intends to address the country's smoking problem by imposing higher taxes on tobacco products.[2]

Tobacco industry is a substantial source of income for many Filipinos especially in the northern region of the country. Despite significant tobacco production, local tobacco farmers and legitimate tobacco product manufacturers are suffering economically, according to Cervantes (2022)[3], because of the high tax and the vast amount of tobacco goods smuggled into the country by illegal importers and merchants.

There has been a notable surge in the illicit tobacco traffic in recent years. Gonzales (2023) reports that the Philippines lost Php26.19 billion in revenue in 2022 alone, which could have been used to finance housing, medical, and educational initiatives, among others. Illicit manufacturing, counterfeit production, smuggling, and bootlegging include buying cigarettes in bulk from low-tax countries to sell them in high- tax countries. The Philippine Star reported on November 24, 2023 that illicit tobacco trafficking cost P60 billion in taxes for 2023[4]. The Bureau of Internal Revenue defines the four fundamental types of illicit tobacco trade as illicit manufacturing, counterfeit production, smuggling and bootlegging. With the current technology it is difficult to monitor illicit manufacturing of tobacco.[5] At present, twelve policies have been established with the aim of preventing the illicit tobacco trade; nevertheless, a significant portion of these policies remain unimplemented.

[1] WHO Fact Sheet, published July 31, 2023

[2] The Sin Tax Reform Act of 2012 or R.A. 10351 was signed into law on December 19, 2012

[3] Cervantes, F. (2022, November 15). Gov't loses P26B in revenue yearly due to illicit tobacco trade. Philippine News Agency. (https://www.pna.gov.ph/articles/1188668)

[4] Philippine Star. https://www.philstar.com/business/2023/11/24/2313704/

[5] BIR: P60 billion taxes lost to illicit tobacco trade. (2023, November 23). The Philippine Star. https://www.philstar.com/business/2023/11/24/2313704/bir-p60-billion-taxes-lost-illicit-tobacco-trade

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Review Question

This systematic review aims to answer the following research question:

"What are the differences of heavy metal concentration between illicit and registered cigarette brands and their potential health effects?". Stating the question allows a structured approach in the search strategy, selection criteria and synthesis of evidence. Clear definition of the review question is important in maintaining the focus of the study and ensuring that included studies will directly contribute in assessing the primary objective.

Objectives of the Study

General objective: To assess the concentrations of different heavy metals in both illicit and registered cigarettes and their potential effects on human health.

Specific objectives:

- To determine the specific heavy metals present in illicit and registered cigarettes.
- To determine the impact on human health of heavy metals in cigarettes.
- To determine the immediate and long-term health consequences of heavy metals present in both illicit and registered cigarettes

Methodology and Research Strategy

A comprehensive search was done to search relevant studies published in between 2019 and 2023 from electronic databases, such as Cochrane Library, Google Scholar, and PubMed. The electronic search utilized a combination of terms including "heavy metals", "toxic metals" and "Illicit cigarette", "registered cigarette", "cigarette", "tobacco", and "health effects", "lung function" in addition to the controlled vocabulary such as MeSH terms or other subject phrases, synonyms, and search filters. To maximize the retrieval of other relevant studies, Boolean operators (i.e. AND, OR) were also applied. The broad search ensured the inclusion of studies such as randomized controlled trials, observational studies and systematic reviews. There were no limitations on the type of publication or the language used. In addition, a manual examination was conducted on the reference lists of the studies. This approach enhanced the completeness of the review, ensuring that all pertinent studies related to heavy metal concentration in cigarettes and its potential health effects were included.

Two reviewers (E.C. and G.S.) screened the studies for risk of bias. All titles, abstracts and full texts were reviewed using a standardized form. Critical appraisal was done using Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool, used depending on the type of study. This ensured that the quality of the study was assessed eliminating the bias. The discrepancies were resolved by consensus. The independent and duplicated process increased the subjectivity and decreased the subjectivity of the study findings.

A. Eligibility Criteria and Study Selection

This investigation has considered several inclusion criteria. The studies included were selected based on a pre-defined inclusion criterion, with concentration from established electronic databases. The studies that were incorporated in this review were as follows: (i) pertinent randomized controlled trials, case-control studies, observational studies, cohort studies, and systematic reviews (for the purpose of scoping or umbrella reviews); (ii) research involving human

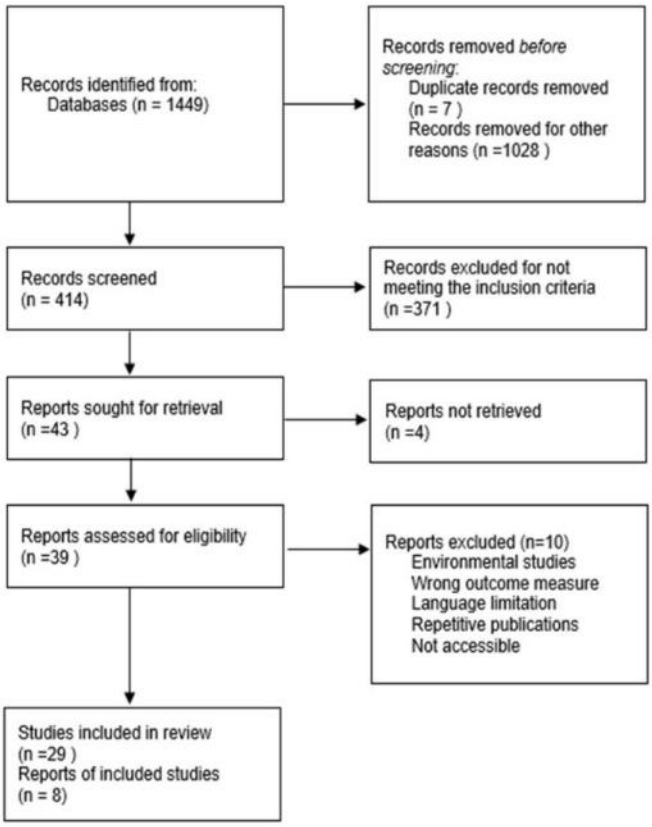
subjects; (iii) laboratory studies; (iv) foreign studies that provided supplementary information; (v) studies examining various heavy metals in cigarettes; (vi) interventions utilizing illicit cigarettes; (vii) controls utilizing registered cigarettes; and (viii) outcomes of interest were included. A comprehensive evaluation of each study was conducted using appropriate resources to guarantee the quality of the evidence. The Cochrane Risk of Bias Tool was utilized for randomized controlled trials and then Newcastle-Ottawa Scale was utilized for observational studies. As a result of this combination, possible biases in the literature were fully addressed during the appraisal process.

B. Risk of Bias

The risk of bias was evaluated for each study in accordance with the domains specified in the Cochrane Handbook for Systematic Reviews of Interventions: Random Sequence generation (Selection Bias), Allocation Concealment (Selection Bias), Blinding of Outcome Assessment (Attrition Bias), Incomplete Outcome Data (Attrition Bias), and any other source of bias. Research studies with a low risk of bias in all relevant domains or in which bias altering outcomes appear unlikely were considered low-risk and were included in the study.

A template developed by Cochrane Collaboration for data extraction of both RCTs and non-RCTs in a systematic review was used for independent, duplicate data extraction. This was used to reduce bias and errors. A pilot phase was done and reviewers were informed regarding how to utilize the form, this ensures uniformity. The important data that were extracted from each study were study design, sample size, demographics and results pertaining heavy metal concentrations and potential health effects. Duplicate extraction procedure was also done to guarantee the validity and dependability of the review.

Figure 1: Flowchart for identifying references for inclusion in systematic review.



Results

The results of the searches yielded eight pertinent studies. Table 1 contains a summary of the studies that were included. The main findings of the included studies regarding the heavy metal content of both illicit and legal cigarettes were compiled using a narrative synthesis.

Table 1. Included Studies

Author, Year, Country	Objective	Population	Results
Ozcan (2019) (Turkey)	To determine heavy metal and macroelement distribution in Turkish-used Indian and imported cigarette brands.	N=26 Five Indian cigarettes vs twenty-one imported cigarettes.	Imported cigarettes are higher in Fe and Mn than Indian cigarettes.
Janaydeh (2019) (Malaysia)	To assess the toxicity of Pb and Cd in 15 tobacco cigarette brands in Selangor, Peninsular Malaysia.	N=10 Fifteen different brands of tobacco cigarettes were purchased from several markets in January 2016 from Selangor state, Malaysia	Pb and Cd contents varied significantly between tobacco cigarette brands and costs.
Pappas (2006) (USA)	To evaluate counterfeit cigarette smoke particle cadmium, lead, and thallium to legitimate US brands.	N=27 Six authentic cigarette brands and twenty-one counterfeit cigarettes.	All counterfeit brands had Greater main smoke particulate cadmium levels than authentic brands.
He (2015) (USA)	To examine US counterfeit cigarette lead and cadmium concentrations.	N=27 Four authentic cigarette brands and twenty-three counterfeit cigarettes.	Pb and Cd concentrations in counterfeit cigarettes were much higher and more variable.
Strungaru (2018) (Roumania)	To detect toxic metal levels of cadmium, lead, cooper, chromium, and nickel in filler tobacco from common cigarette brands obtained from Iaşi City's local and black (illegal) markets.	N=240 Eight different brands were common to every legal shop and black market.	Cadmium and lead concentrations were much greater in black market brands.
Swami (2009) (USA)	To measure trace levels of Be, V, Cr, Mn, Co, Ni, Cu, Zn, As, Se, Mo, Cd, Sb, Ba, Tl, and Pb in cigarette tobacco samples	N=5 Two sets were authentic cigarettes and 3 sets were counterfeit cigarettes.	Counterfeit cigarettes had much higher concentrations of Be, Mn, As, Se, Mo, Cd, Tl, Pb, and Hg than authentic cigarettes.
Ajab (2008) (Pakistan)	To determine the heavy metal content of local and imported cigarette brands used in Pakistan	N=20 Twenty cigarette brands in Pakistan were tested using flame atomic absorption spectrophotometry	The analysis showed that imported brands had the highest concentrations of Mn (84.78 microg/g dry weight), Cd (0.525), and Zn (14.34).
Lisboa (2020) (Brazil)	To compare chromium contents in tobacco, filter, and cigarette ash samples using electrothermal vaporization– atomic absorption spectrometry (ETV-AAS) and sample preparation methods.	N=12 Twelve cigarette samples (different brands) of illicit origin were obtained from a local market with standard reference material of tomato leaves.	Mean Cu and Pb values in contraband cigarette samples were 19.6 and 7.5 µg g-1, respectively.

As shown in the table 1 above, Cadmium and lead concentrations in illicit and registered cigarettes were investigated in four separate studies. Strungaru (2017) measured toxic metals in filler tobacco from typical cigarette brands from the local market as well as the black market in Laşi City, Romania. Results showed that black market brands had much higher cadmium and lead contents. Legal market brands had substantially higher copper levels. He (2015) investigated US counterfeit cigarettes from China, Paraguay, and some unknown sources. Pb and Cd levels were significantly higher in 22 of 23 counterfeit cigarette samples than in equivalent genuine brands. Swami (2009) demonstrated that the levels of Be, As, Mo, Cd, Sb, Tl, Pb, and Hg are greater in counterfeit cigarettes. On the other hand, the levels of V, Cr, Mn, Co, Cu, Zn, Se, and Ba are equivalent between legal and counterfeit cigarettes. Interestingly, registered cigarettes have 2.7-fold higher Ni. The samples were from two genuine and three counterfeit cigarette packs. The mean Pb content of counterfeit cigarettes was 5.69 mg, nearly 10 times that of registered cigarettes. Pappas (2006) examined 21 counterfeit cigarette samples for toxic heavy metals. The findings of the study indicated that

counterfeit cigarettes may pose a significantly higher risk of toxic heavy metal exposure compared to authentic brands, even when nicotine intake differences were accounted for.

Two studies compared local and imported cigarettes. Ajab (2008) showed increased concentrations of Mn, Zn, and Cd were detected in cigarettes that were imported, whereas local brands contained higher concentrations of Co, Pb, and Cu. A study by Özcan (2019) analyzed the heavy metal and macroelement levels of Indian and imported cigarettes in Turkey. The findings indicate that cigarette samples imported from India and utilized in Turkey are abundant in Ca, K, Mg, P, and S. The majority of imported cigarettes contained elevated levels of Cu and Cd in comparison to Indian cigarettes. Janaydeh (2019) showed the Pb and Cd content of different tobacco brands in Selangor state, Peninsular Malaysia.

The study compared cheap versus expensive cigarettes. The Pb and Cd contents varied significantly between tobacco cigarette brands and cost. However, the highest Pb levels were found in cheap tobacco samples and the lowest in expensive samples.

Lisboa (2019) demonstrated that illegal brands have higher harmful element concentrations than genuine brands. Mean concentrations of Cu and Pb in tobacco for the samples of illegal cigarettes in this study were 19.6 and 7.5, respectively.

According to the findings of the study, tobacco cigarettes are one of the primary sources of extremely hazardous heavy metals, including cadmium and lead. These heavy metals are just one of numerous types of compounds that are hazardous, carcinogenic, and addicting that can be found in smoke.

DISCUSSION

Tobacco use is a major risk factor for cancer in almost any part of the body but commonly lung cancer and cardiovascular illnesses. This is due to the weakening of the immune system and direct DNA damage causing uncontrolled cell proliferation. Individuals who are not smokers but are exposed to secondhand smoke also endure the detrimental health consequences associated with tobacco use. Chronic second hand smoke exposure causes lung cancer, coronary heart disease, and respiratory issues.

Majority of the studies show counterfeit cigarettes have significant cadmium and lead levels. Cadmium and lead levels in smokers and non-smokers were examined by Repic (2019)[6]. Smokers have 3.5 and 1.5 times higher blood of cadmium and lead than non- smokers. Smoking habits like number of cigarettes per day, smoking period, cigarette type, and age affected these metals' blood concentrations. Smoking 10 cigarettes a day for 10 years showed significant elevation for blood levels of Cd and Pb. Low-concentration cadmium is hazardous, while lead have both acute and cumulative toxicity. Cadmium overexposure causes acute and chronic poisoning leading to pulmonary edema pneumonitis, acute respiratory distress syndrome from direct destruction of the mucus membrane and acute renal injury through cadmium-matallothionin complex where it burdens the renal tubules and causes damage. On the other hand, lead exposure can damage the nervous system being a neurotoxin, especially in young children, who can acquire learning problems at low levels. This happens thru the production of reactive oxygen species causing oxidative stress causing lipid peroxidation which damages cell membrane causing cell destruction. In adults in can cause paralysis, encephalopathy, coma or even death due to its prolonged half-life of 2 to 3 years in the brain.

The unregulated tobacco growing environment likely causes excessive heavy metal concentrations in counterfeit cigarettes together with poor preparation due to lack of standards and

[6]Repić, A., Bulat, P., Antonijević, B., Antunović, M., Džudović, J., Buha, A., & Bulat, Z. (2019).

quality assurance control. Heavy metal enrichment in cigarettes also depends on soil pH, according to Golia (2007)[7]. Growth of tobacco on severely acidic soil can increase cadmium and other heavy metals by fivefold. Because of quality control measures, major tobacco producers ceased employing these crops, potentially leading to the adoption of them by counterfeit enterprises. Tobacco quality is regulated by major manufacturers of genuine brands in response to environmental conditions. Thus, genuine brands have stable heavy metal content. Cadmium and lead are constantly regulated in cigarette manufacture, according to four studies.

Lack of control over cigarette manufacture and international mobility drives the global trade in illicit tobacco products. This trade is run by illegal organizations that have sophisticated systems for distributing illicit and counterfeit cigarettes. It happens in low- and high-tax jurisdictions. Developing nations have greater illicit trade.

Despite the insights of the current review, limitations such as small sample size and cross-sectional designs in some included studies call for additional research. Future research may aim to conduct well-powered studies or randomized controlled trials to assess further the long-term health effects of heavy metal exposure from cigarette smoke. Investigations regarding the regulatory impact on reducing heavy metal content in cigarettes may be considered since it will also help public health policies. (Lisboa et al., 2020; Dahlawi et al., 2021).

This study confirmed that counterfeit cigarettes present a more significant health hazard in comparison to authentic cigarettes. Accordingly, the public health risks of the illegal cigarette trade increase with counterfeit cigarette market share.

RECOMMENDATIONS

Due to the health risks associated with heavy metals, monitoring of heavy metals throughout the tobacco-growing, refining, and smoking processes should be subject to stringent quality control. Given the prevalence of smoking, epidemiological research on human metal exposure should account for cigarette smoke, therefore minimizing hazardous exposure is essential. The findings of the studies imply that the cigarette market needs proper oversight to protect consumers' health and safety.

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