



REVIEW

## The association between smoking behaviour and degenerative diseases

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### ABSTRACT

Degenerative diseases represent a leading global cause of death, imposing a substantial health burden, wherein behavioural factors such as smoking are posited to play a significant role. This study aimed to analyse the association between smoking behaviour and the incidence of various degenerative diseases through a systematic literature review. The methodology employed was a systematic literature review, with article searches conducted across Google Scholar, PubMed, and Scopus databases from May to June 2025. Inclusion criteria encompassed full-text articles in Indonesian or English, published between 2020 and 2025, focusing on the association between smoking and degenerative diseases (hypertension, diabetes, stroke, kidney failure, cancer). From 230 identified articles, 15 met the criteria and were analysed. The synthesis of results demonstrated a significant association between smoking behaviour and an increased risk of degenerative diseases. Active smokers exhibited a three-fold higher risk of hypertension (OR=3.445), a twelve-fold higher risk of type 2 diabetes mellitus (OR=12.747), and a greater risk of developing cancer (lung, breast, laryngeal), stroke, and chronic kidney disease (CKD). Exposure to secondhand smoke among passive smokers also increased the risk of breast cancer nearly fourfold (OR=3.778). Underlying mechanisms include oxidative damage, chronic inflammation, endothelial dysfunction, and metabolic dysregulation. It is concluded that smoking is a major modifiable risk factor for degenerative diseases. Strengthening tobacco control policies, intensive health education, and smoking cessation programmes are required as primary prevention strategies.

**Keywords:** tobacco, degenerative diseases, hypertension, diabetes, cancer

### Introduction

Degenerative diseases, characterised by the progressive and chronic decline of organ function, have become a global health burden with significant mortality.<sup>1</sup> Annually, nearly 17 million people die prematurely due to the epidemic of degenerative diseases such as hypertension, diabetes mellitus, stroke, and chronic kidney failure.<sup>2</sup> The shift in disease patterns from communicable to non-communicable, exacerbated by lifestyle changes including unbalanced diets and low physical activity, has led to an increased prevalence of degenerative diseases, particularly in developing countries and ageing populations.<sup>3</sup> Among various behavioural risk factors, smoking habit stands out as a major contributor that accelerates organ degeneration through oxidative and inflammatory mechanisms.<sup>4</sup>

Globally, the World Health Organization (WHO) reports over 1.3 billion active smokers, with approximately 1.2 million annual deaths among passive smokers due to secondhand smoke exposure.<sup>5</sup> The situation in Indonesia is particularly concerning, where data from Riskesdas 2018 and the Global Adult

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Tobacco Survey (GATS) 2021 indicate that around 33.5% of the population aged  $\geq 15$  years are active smokers, with a prevalence exceeding 60% among males.<sup>6</sup> More alarmingly, over 70% of children and women are exposed to tobacco smoke in household environments, placing them at significant long-term health risk as passive smokers.<sup>6</sup> The duration and intensity of smoking play a crucial role; individuals who have smoked for more than ten years possess a two- to three-fold higher risk of developing hypertension, stroke, lung cancer, and chronic kidney failure compared to non-smokers.<sup>7</sup>

Tobacco smoke contains over 7,000 chemical compounds, including nicotine, tar, carbon monoxide, and various carcinogens.<sup>8</sup> These substances trigger cellular damage through oxidative stress, chronic inflammation, vascular endothelial dysfunction, and DNA damage, ultimately accelerating cellular ageing and inducing degenerative diseases.<sup>9</sup> The causal link between smoking and diseases such as lung cancer, coronary heart disease, and chronic obstructive pulmonary disease is long-established.<sup>10</sup> However, a comprehensive review of its role in a broader spectrum of degenerative diseases (such as diabetes, hypertension, CKD, stroke, and various cancers) and the underlying biological mechanisms requires further consolidation, particularly within the context of recent research evidence from Indonesia.

Based on this urgency, this study was conducted to analyse the association between smoking behaviour and degenerative diseases through a systematic literature review. Its specific objectives were to: 1) Identify the types of degenerative diseases most influenced by smoking habit; 2) Explain the biological and physiological mechanisms by which smoking accelerates the degeneration process; and 3) Examine other risk factors that interact with smoking in the development of degenerative diseases. The findings of this review are expected to provide a robust scientific foundation for developing more effective public health policies and intervention programmes in tobacco control and degenerative disease prevention in Indonesia.

## Method

This study employed a systematic literature review design to examine and synthesise current scientific evidence regarding the association between smoking behaviour and degenerative diseases.<sup>11</sup> A systematic literature search was conducted from May to June 2025 across three scientific databases: Google Scholar, PubMed, and Scopus. The search keywords used were combinations of: ("Degenerative Diseases") AND ("Smoking") along with specific disease keywords: "Hypertension", "Diabetes", "Kidney Failure", "Stroke", "Cancer". The initial search yielded 230 potentially relevant articles.

The article selection process was conducted in stages by applying predetermined inclusion and exclusion criteria. Inclusion criteria comprised: (1) National or international journal articles discussing the association between smoking behaviour and degenerative diseases; (2) Study subjects involving active or passive smokers; (3) Available in full-text format; (4) Published in Indonesian or English; (5) Publication year between 2020 and 2025; (6) Degenerative diseases studied included hypertension, diabetes mellitus, chronic kidney failure, stroke, or cancer. Exclusion criteria were: (1) Articles not discussing the direct association between smoking and degenerative diseases; (2) Available only in abstract form; (3) Published before 2020; (4) Comprising seminar reports, proceedings, or theses without journal peer-review.

After duplicate removal (150 articles), screening based on title and abstract was performed on 80 articles, resulting in 50 articles deemed relevant. A full-text evaluation of 30 articles was then conducted, and 15 final articles meeting all inclusion criteria and possessing adequate methodological quality were selected for synthesis in this review. This selection flow followed a modified PRISMA diagram. Data from each selected study were extracted into a table containing information on authors, year, title, disease subject, research method, key results (including statistical measures such as p-value and Odds Ratio/OR), and source database. Analysis was performed narratively by synthesising findings from various studies to identify patterns, strength of associations, and consistent mechanisms.

## Results

Based on the systematic selection process, 15 journal articles met the criteria and were analysed in this review. The characteristics of these studies are presented in Table 1. The majority of the research ( $\geq 10$  studies) used a cross-sectional design, while the remainder were analytical observational studies and one utilised a logistic regression model. The publication years ranged from 2020 to 2025, with a focus on various degenerative diseases in Indonesia.

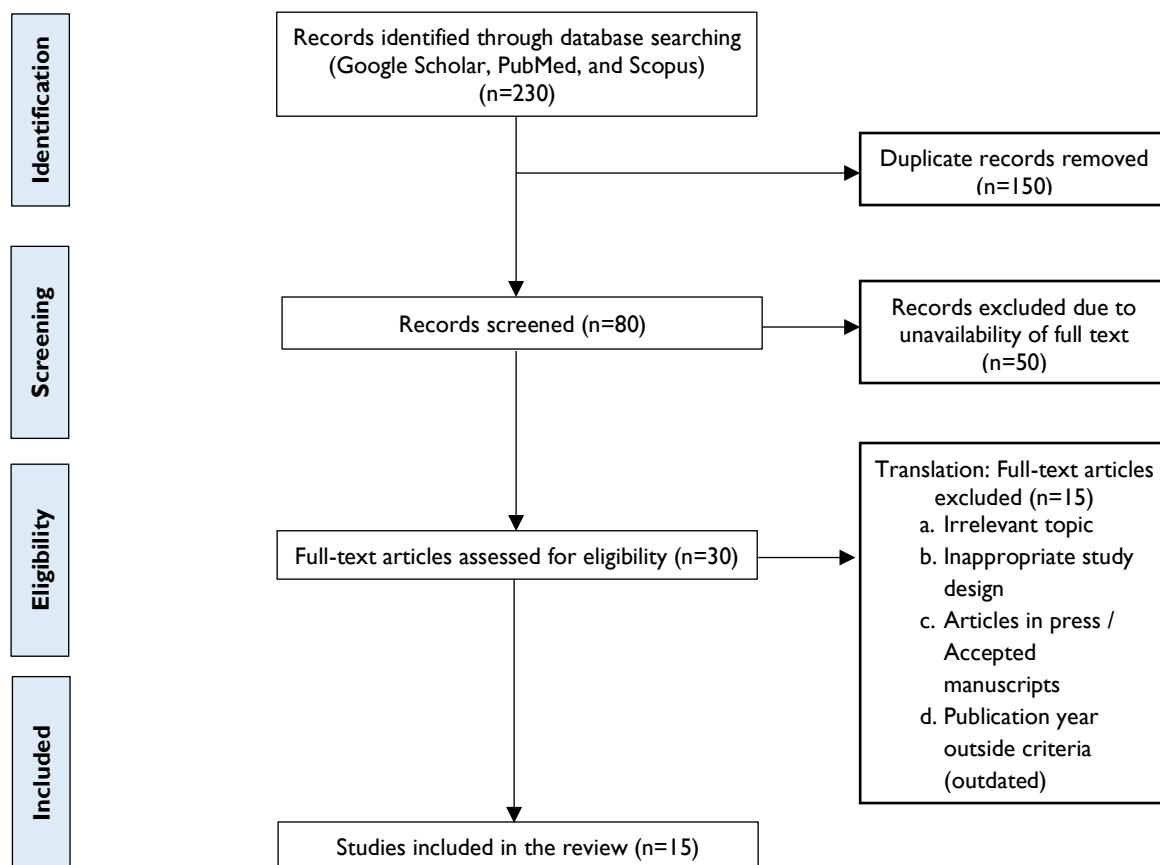


Figure 1. Flowchart of search results and study selection

The synthesis of results from these 15 studies revealed several key findings. First, smoking significantly increases the risk of various cancers. The study by Puspawati et al. (2020) estimated that smoking causes 59,071.6 Years of Life Lost (YLL) in Indonesia, with lung cancer as the largest contributor.<sup>12</sup> The risk of lung cancer was also confirmed by Patola & Tridiyawati (2024).<sup>20</sup> Beyond lung cancer, smoking is also associated with laryngeal cancer (Anisah et al., 2024),<sup>22</sup> and exposure to secondhand smoke (passive smoking) increases breast cancer risk with an OR of 3.778 (Paratiwi, 2021)<sup>17</sup> and in younger women (Ambarita et al., 2024).<sup>19</sup> However, one study (Pranitia et al., 2021) found a statistically non-significant association between smoking history and cervical cancer, although the OR value indicated a trend towards increased risk (OR=4.324).<sup>14</sup>

Second, a strong association is evident between smoking and metabolic and cardiovascular diseases. Smoking increases the risk of hypertension in the productive age group with an Odds Ratio of 3.445 (Prameswari et al., 2023; Dilla et al., 2024).<sup>18,23</sup> Furthermore, smoking is a dominant risk factor for type 2 diabetes mellitus, where smokers have a twelve-fold higher risk (OR=12.747) compared to non-smokers (Anggoro et al., 2025).<sup>26</sup> Smoking habit also worsens chronic complications in diabetic patients (Sastrawan et al., 2023).<sup>16</sup>

Third, the impact of smoking on the cerebrovascular and renal systems is also evident. Smoking is a strong predictor of stroke incidence (Al Raffi & Purnomo, 2024) and correlates with higher stroke severity (Patola & Tridiyawati, 2024).<sup>21,24</sup> In chronic kidney disease (CKD), smoking acts as a risk amplifier that strengthens the risk of cardiovascular events and mortality (Provenzano et al., 2021), and its direct association with CKD incidence is also significant (Ariani et al., 2024).<sup>13,25</sup>

Overall, a consistent pattern emerges indicating that both active smoking and exposure as a passive smoker increase the risk of degenerative diseases. This relationship exhibits a dose-response pattern, where the duration and intensity of smoking are directly proportional to the increased risk. The majority of studies show p-values <0.05 and Odds Ratios (OR) above 1, indicating a significant strength of association.

## Discussion

This systematic review confirms that smoking behaviour is a major modifiable risk factor for a broad spectrum of degenerative diseases, including cancer, cardiometabolic, cerebrovascular, and renal diseases. The consistent findings from various cross-sectional and observational studies in Indonesia align with global evidence positioning smoking as a leading cause of morbidity and premature mortality.<sup>5,8</sup>

The pathophysiological mechanisms underlying this association are complex and multifactorial. First, tobacco smoke contains thousands of toxic and carcinogenic compounds (such as nitrosamines, polycyclic aromatic hydrocarbons) which can cause direct DNA damage, genetic mutations (e.g., in the p53 gene), and inhibition of apoptosis, thereby triggering cancer initiation and progression.<sup>22,27</sup> Second, nicotine and carbon monoxide induce sympathetic nervous system activation, vasoconstriction, vascular endothelial dysfunction, and accelerated atherosclerosis.<sup>9,23</sup> These processes explain the increased risk of hypertension, heart disease, and stroke, including the correlation between smoking duration and stroke severity found in this review.<sup>24</sup> Third, smoking induces a state of oxidative stress and chronic systemic inflammation. This condition contributes to insulin resistance, pancreatic beta-cell dysfunction, and impaired glucose metabolism, forming the biological basis for the markedly higher risk of type 2 diabetes mellitus among smokers (OR=12.747).<sup>26,28</sup> Fourth, in the kidneys, toxic substances from tobacco can cause direct glomerular damage, while its systemic effects (hypertension, atherosclerosis) increase renal workload. Provenzano et al. (2021) demonstrated that smoking amplifies other risk factors such as proteinuria in CKD patients, accelerating progression towards end-stage renal disease.<sup>13</sup>

Table 1. Summary of study findings

No	Author & Year	Title/Study Focus	Key Findings	Effect Size/Statistics
1	Puspawati et al. (2020)	Impact of Smoking on Premature Death (YLL) from Cancer	Smoking causes the greatest loss of productive life years from lung, liver, and bladder cancer.	Total YLL = 59,071.6 years; YLL lung cancer males = 27,213. <sup>12</sup>
2	Provenzano et al. (2021)	Smoking & Cardiovascular Risk in CKD	Smoking amplifies the risk of cardiovascular complications and mortality in CKD patients.	CV risk 1.93x, mortality risk 2.13x; each additional cigarette/day ↑ risk 4%. <sup>13</sup>
3	Pranitia et al. (2021)	Smoking & Cervical Cancer	Smoking history increases cervical cancer risk in women >35 years.	Risk 4–13x higher, p=0.000; r=0.722. <sup>14</sup>
4	Choirunnisa et al. (2022)	Smoking & Diabetes Mellitus	A significant association exists between smoking habit and DM incidence.	p=0.039. <sup>15</sup>
5	Sastrawan et al. (2023)	Smoking & Chronic Complications in Type II DM	Smoking behaviour is associated with increased chronic complications in type 2 DM.	p<0.01. <sup>16</sup>
6	Paratiwi (2021)	Passive Smoking & Breast Cancer	Passive smokers have a higher likelihood of developing breast cancer.	OR=3.778, p=0.003. <sup>17</sup>
7	Prameswari et al. (2023)	Smoking & Hypertension in Productive Age	Smoking increases the likelihood of hypertension in the productive age group.	OR=3.445, p<0.05. <sup>18</sup>
8	Ambarita et al. (2024)	Secondhand Smoke Exposure & Breast Cancer in Young Age	Secondhand smoke exposure >10 years increases breast cancer risk in women <40 years.	92% of cases were passive smokers, p=0.016. <sup>19</sup>
9	Patola & Tridiyawati (2024)	Smoking & Lung Carcinoma	Smoking history significantly influences lung cancer incidence.	p=0.000; significant OR. <sup>20</sup>
10	Al Raffi & Purnomo (2024)	Smoking as a Predictor of Stroke	Smoking increases stroke risk through vascular mechanisms.	Smoking is a strong modifiable risk factor. <sup>21</sup>
11	Anisah et al. (2024)	Smoking & Laryngeal Cancer	A significant association exists between smoking and laryngeal cancer.	p=0.025. <sup>22</sup>
12	Dilla et al. (2024)	Smoking Behaviour & Hypertension	Smoking increases hypertension risk in the productive age group.	p=0.001. <sup>23</sup>
13	Patola & Tridiyawati (2024)	Smoking & Stroke Severity	Long-term smoking is related to more severe stroke outcomes.	p=0.024; r=0.444 (moderate correlation). <sup>24</sup>
14	Ariani et al. (2024)	Smoking & CKD	Smokers have a higher proportion of CKD compared to non-smokers.	p=0.001. <sup>25</sup>
15	Anggoro et al. (2025)	Smoking & Type 2 DM in the Elderly	Smoking is the most dominant factor for type 2 DM incidence in the elderly.	OR=12.747, p=0.020. <sup>26</sup>

The findings regarding breast cancer in passive smokers (OR=3.778) and in young women (<40 years) are crucial from a public health perspective.<sup>17,19</sup> This indicates that the dangers of tobacco are not confined to active smokers. Environmental tobacco smoke contains concentrations of carcinogens that are also harmful.<sup>20</sup> Young women exposed at home or the workplace are at significant risk, demanding stronger protection through stricter smoke-free area policies.

While the majority of results show significant associations, the finding by Pranitia et al. (2021) that smoking history was not statistically significant for cervical cancer ( $p=0.356$ ) requires careful interpretation.<sup>14</sup> The large OR value (4.324) suggests a potential association, but statistical power may have been limited by sample size. Major confounding factors such as Human Papillomavirus (HPV) infection, the primary cause of cervical cancer, may have a more dominant influence and could obscure the independent relationship with smoking. However, biologically, tobacco metabolites accumulated in cervical mucosa can act as co-factors in carcinogenesis by increasing cellular susceptibility to DNA damage from HPV.<sup>29</sup>

This review has several limitations. First, the majority of included studies employed a cross-sectional design, thus precluding definitive causal inference; they only demonstrate associations at a single point in time. Second, there was variation in the measurement of the "smoking behaviour" variable (e.g., smoking status vs. intensity vs. duration) across studies, which may affect the comparability of results. Third, the focus on Indonesian and English-language literature from specific databases may have omitted relevant studies from other sources. Fourth, publication bias, whereby studies with significant results are more likely to be published, may have influenced the synthesis of findings.

Nevertheless, the consistency of findings across studies with different populations and settings strengthens the validity of the conclusions. The implications of this review are clear: efforts to prevent degenerative diseases in Indonesia must place tobacco control as a top priority. Interventions should be multisectoral, encompassing health education on the dangers of active and passive smoking, smoking cessation counselling, the establishment and enforcement of smoke-free areas, and fiscal policies such as increased tobacco excise taxes.

## Conclusion

Based on a systematic literature review of 15 research articles, it is concluded that a significant and meaningful association exists between smoking behaviour and an increased risk of various degenerative diseases, including hypertension, type 2 diabetes mellitus, stroke, chronic kidney disease, and various cancers (lung, breast, laryngeal). This risk applies not only to active smokers but also to passive smokers exposed to environmental tobacco smoke. Underlying mechanisms involve oxidative damage, chronic inflammation, vascular endothelial dysfunction, metabolic disorders, and carcinogenesis. Smoking is a modifiable risk factor; therefore, smoking cessation efforts and prevention of smoking initiation must be core strategies in degenerative disease prevention programmes. It is recommended that the government and policymakers strengthen comprehensive tobacco control regulations, enhance public health education regarding the adverse effects of smoking, and provide broader access to smoking cessation services. For future research, conducting longitudinal or cohort studies is recommended to confirm causal relationships and explore the interaction of smoking with other genetic and environmental factors in the pathogenesis of degenerative diseases.

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