

Effects of Tobacco

Environmental injury, carcinogenesis, and multisystem pathology

Pathology of toxic exposure and systemic disease

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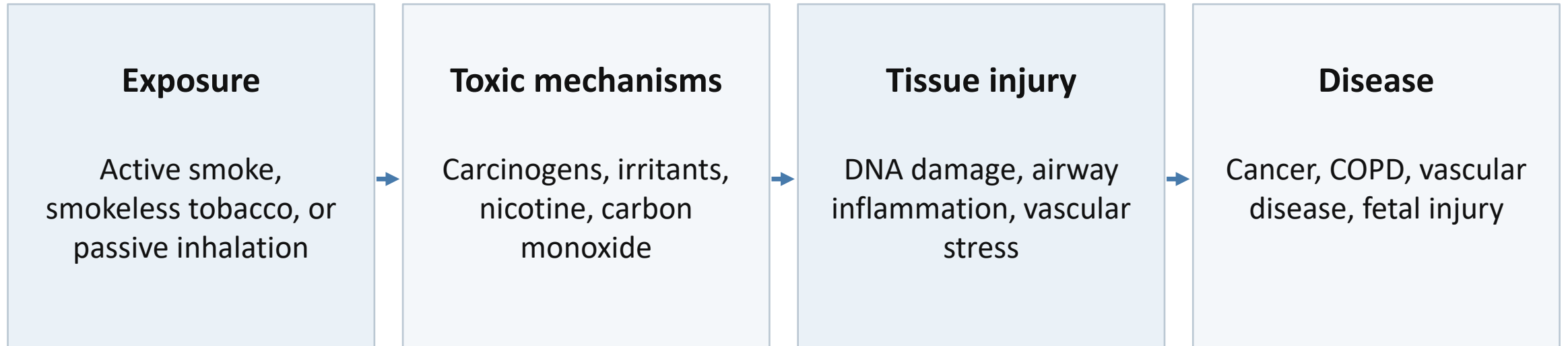
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Teaching objectives

- Identify the principal forms of tobacco exposure and the major affected organs.
- Explain chemical, nicotinic, hypoxic, inflammatory, and genotoxic mechanisms.
- Interpret dose, cumulative exposure, second-hand exposure, and cessation.
- Connect mechanisms to malignancy, lung disease, cardiovascular injury, and fetal effects.

Tobacco injury is a multisystem process



Conceptual pathway · editable schematic

Why tobacco matters in pathology

- Smoking as the most readily preventable cause of death.
- Disease arises in smokers and in nonsmokers exposed to environmental tobacco smoke.
- The same exposure produces malignant and nonmalignant pathologies.
- Risk is shaped by dose, duration, route of exposure, and cessation.

Three clinically important exposure routes

Inhaled cigarette smoke

Direct respiratory mucosal injury

Systemic exposure to smoke constituents

Smokeless tobacco

Oral and mucosal contact with tobacco products

Important association with oral cancer

Second-hand smoke

Inhalation of smoke in a shared environment

Lung, vascular, and childhood respiratory risks

Cigarette smoking is the dominant exposure

- Active inhalation delivers a complex chemical mixture to the airways.
- Absorbed constituents also produce systemic effects beyond the lung.
- Cigarette smoking as the main contributor to tobacco mortality.
- Smoke exposure has both acute physiologic and delayed pathologic effects.

Smokeless tobacco is not harmless

Products

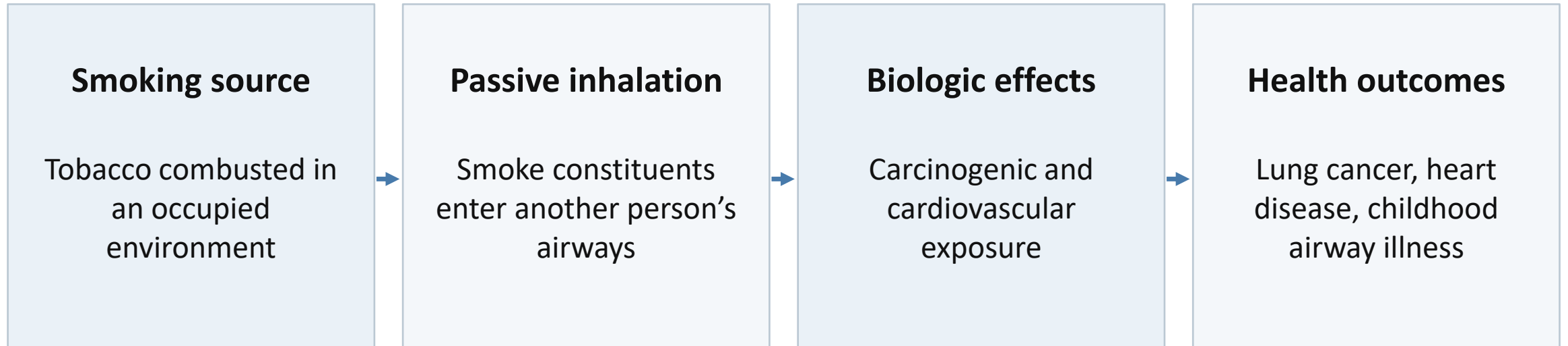
Snuff and chewing tobacco

Pathologic implication

Direct mucosal exposure and increased risk of oral cancer

Absence of smoke inhalation does not imply absence of carcinogenic harm.

Second-hand smoke extends risk to nonsmokers



Conceptual pathway · editable schematic

Global tobacco use: 2023 textbook estimate

≈ 1.3 billion

Smokers worldwide

≈ 5 trillion

Cigarette-equivalents
consumed

$2/3$

Of smokers in 10 countries

Source estimates · interpretation requires the population and period specified in the lecture notes

Tobacco consumption is geographically concentrated

- China leads the list of high-smoking-burden countries in the source.
- India follows, with Indonesia and the United States also listed.
- Russia, Bangladesh, Japan, Turkey, Vietnam, and the Philippines complete the group.
- This concentration focuses the potential impact of population-level prevention.

Smoking prevalence has declined globally

Relative decrease in smoking prevalence, 1990–2020

Males



28%

Females



38%

Scale: 0–40% decrease

Marked declines occurred in several countries

Reported decrease in smoking prevalence, 1990–2020

Brazil



73%

Norway



54%

Senegal



51%

Scale: 0–80% decrease

Tobacco control is linked to prevalence reduction

- Large declines partly to tobacco-control policies.
- The WHO Framework Convention on Tobacco Control provides a multinational policy framework.
- Prevalence trends vary between countries; Falling prevalence is not universal.
- Population exposure and disease burden can remain high despite improvements.

Global mortality burden

>8 million

Tobacco-attributable deaths
per year

≈7 million

Direct tobacco exposure

≈1.3 million

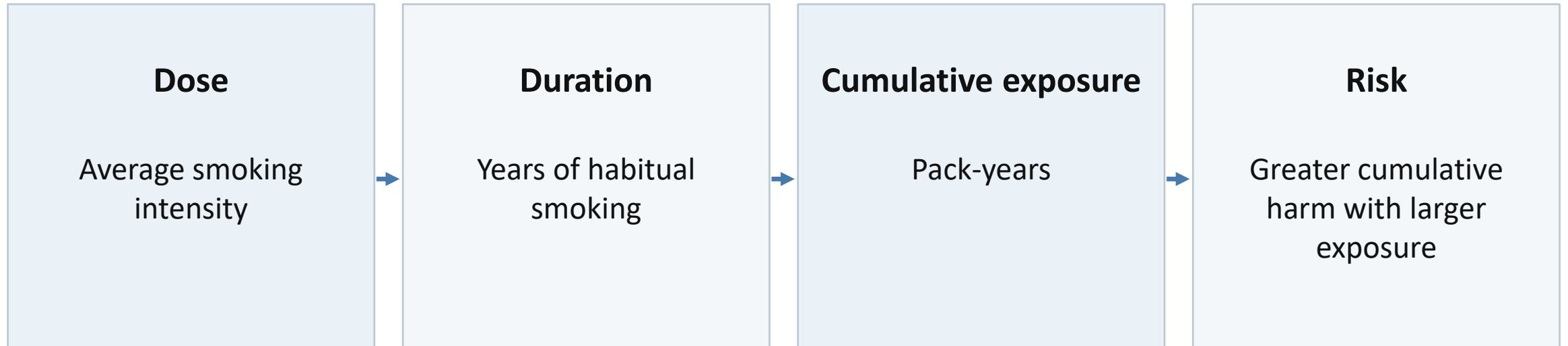
Second-hand smoke exposure

Source estimates · interpretation requires the population and period specified in the lecture notes

Smoking produces preventable premature mortality

- More than 20 million US smoking-related deaths since the 1964 Surgeon General report.
- It attributes almost 2.5 million of those deaths to second-hand smoke.
- Leading causes of tobacco-related deaths include cardiovascular disease, cancer, and chronic respiratory disease.
- These are historical estimates provided by the textbook, not an up-to-date mortality dashboard.

Tobacco harm increases with cumulative exposure



Conceptual pathway · editable schematic

Pack-years quantify cumulative cigarette exposure

$$\text{Pack-years} = \text{packs per day} \times \text{years smoked}$$

- The source defines this as a cumulative exposure measure.
- A pack-year is not a direct biochemical dose of every toxin.
- Always collect both intensity and duration in the smoking history.

Worked clinical exposure example

$$1.5 \text{ packs/day} \times 20 \text{ years} = 30 \text{ pack-years}$$

- The same pack-year figure can arise from different smoking patterns.
- It summarizes cumulative history; It does not determine individual risk by itself.
- Include ongoing smoking or cessation status in the clinical history.

Long-term survival differs in smokers

~75%

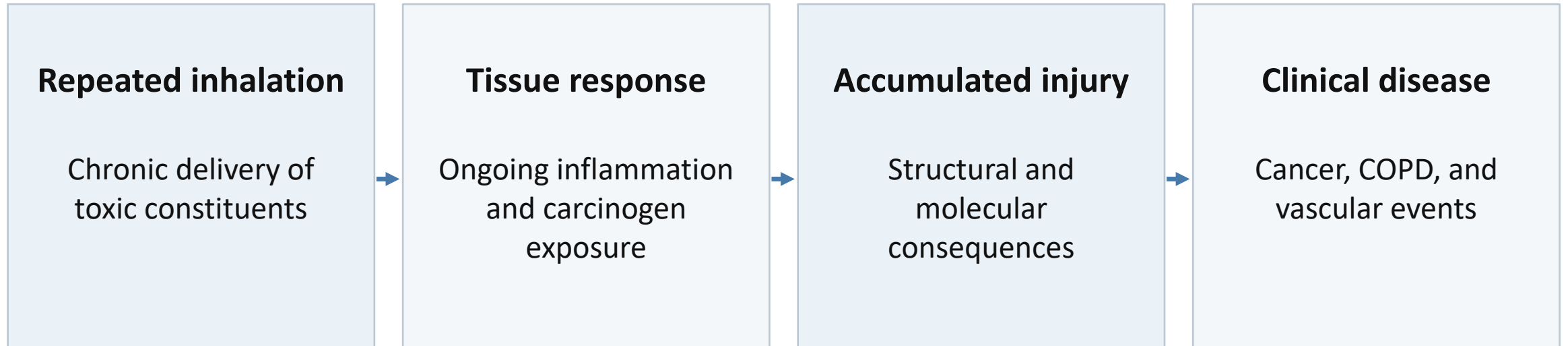
Of nonsmokers reach 70 years

~50%

Of smokers reach 70 years

Source estimates · interpretation requires the population and period specified in the lecture notes

Why cumulative exposure is biologically important

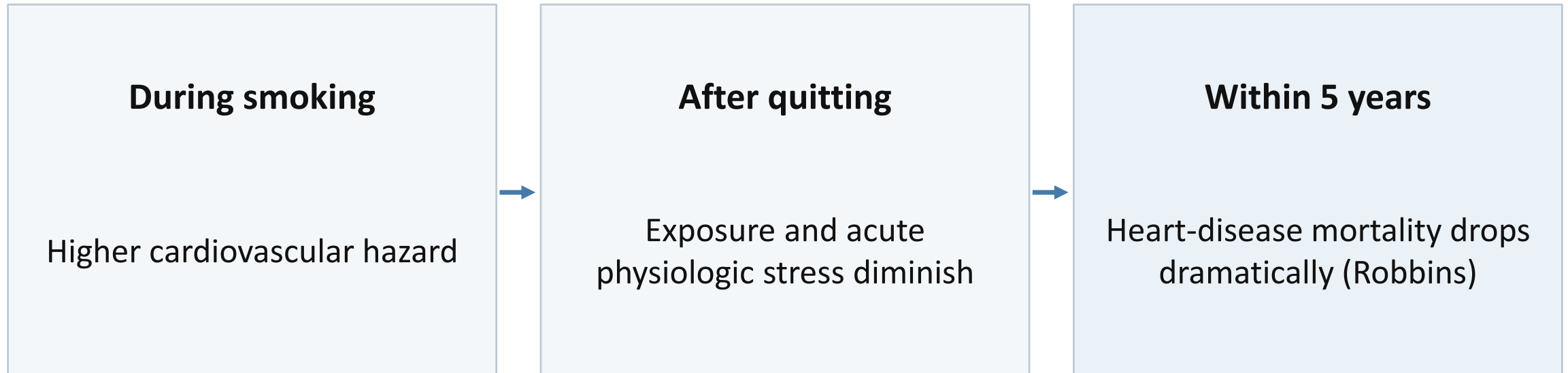


Conceptual pathway · editable schematic

Cessation improves health and lifespan

- The source states that stopping smoking improves overall health and longevity.
- Cardiovascular mortality declines substantially after quitting.
- Lung cancer mortality also falls, but prior exposure creates a prolonged residual excess risk.
- Prevention and cessation therefore complement, rather than replace, clinical surveillance.

Cardiac benefits appear after cessation



Conceptual time course · durations are not drawn to scale

Lung cancer risk persists after quitting



Conceptual time course · durations are not drawn to scale

Cessation has different organ-system time courses

Cardiovascular

Marked mortality improvement within the first 5 years after stopping

Lung cancer

Mortality falls after stopping, but excess risk persists for decades

Pregnancy

Normal infant birth weights when smoking stops before pregnancy

Tobacco smoke is a heterogeneous chemical mixture

$\approx 7,000$

Chemicals in tobacco smoke

> 60

Identified carcinogens

Source estimates · interpretation requires the population and period specified in the lecture notes

Different constituents injure tissues differently

Constituent	Major effect in Robbins
Tar	Carcinogenesis
Polycyclic aromatic hydrocarbons	Carcinogenesis
Nicotine	Autonomic effects; tumor promotion
Phenol	Tumor promotion; mucosal irritation
Carbon monoxide	Impaired oxygen transport and utilization

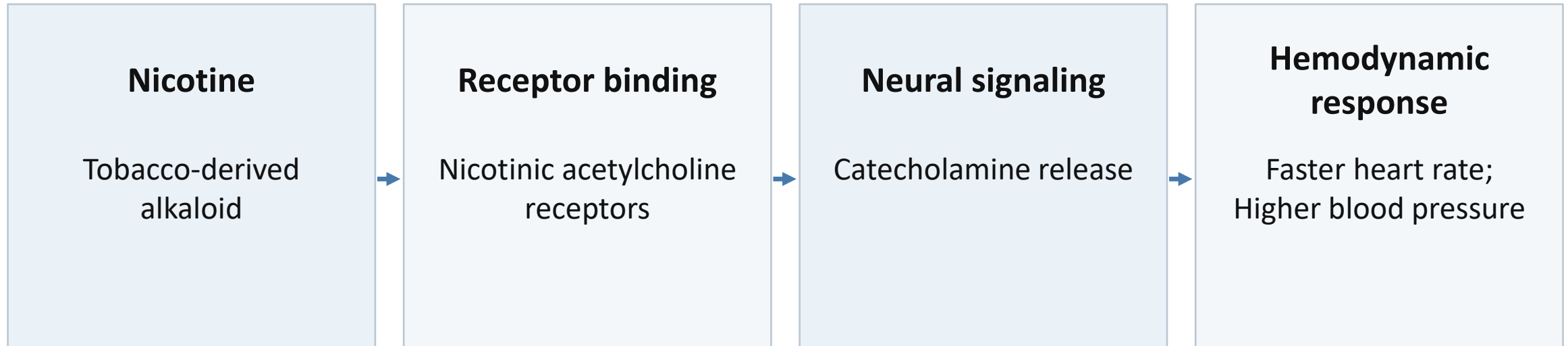
Airway irritants and carcinogens are distinct

Constituent	Major effect in Robbins
Formaldehyde	Ciliary toxicity; mucosal irritation
Nitrogen oxides	Ciliary toxicity; mucosal irritation
Benzo[a]pyrene	Carcinogenesis
Nitrosamines	Carcinogenesis

Nicotine is the major addictive tobacco alkaloid

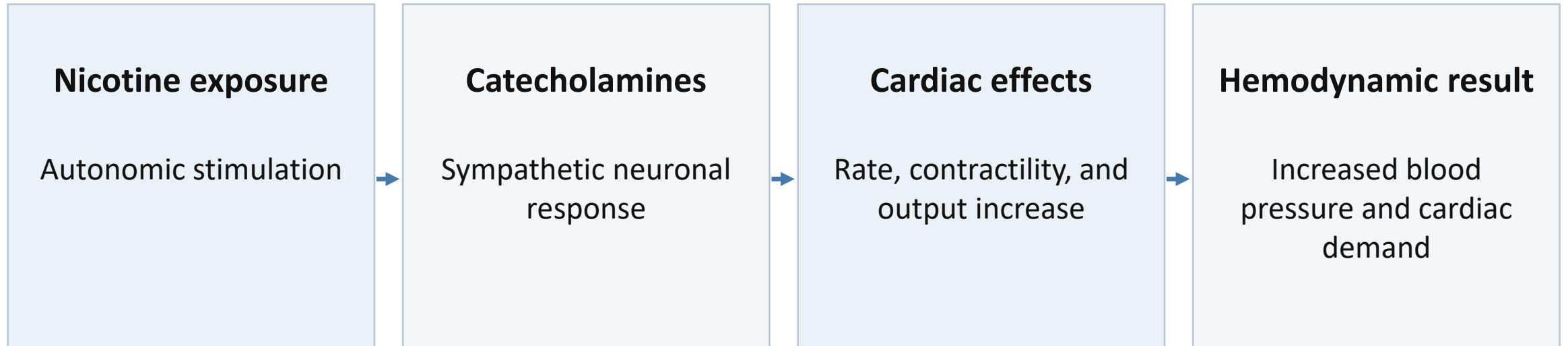
- Nicotine is present in tobacco leaves and is strongly addictive.
- It binds nicotinic acetylcholine receptors in the brain.
- Its autonomic activity provides a mechanism for acute hemodynamic effects.
- Carcinogenic risk from smoke also depends on other constituents.

Nicotinic receptor activation drives acute responses



Conceptual pathway · editable schematic

Nicotine raises myocardial workload

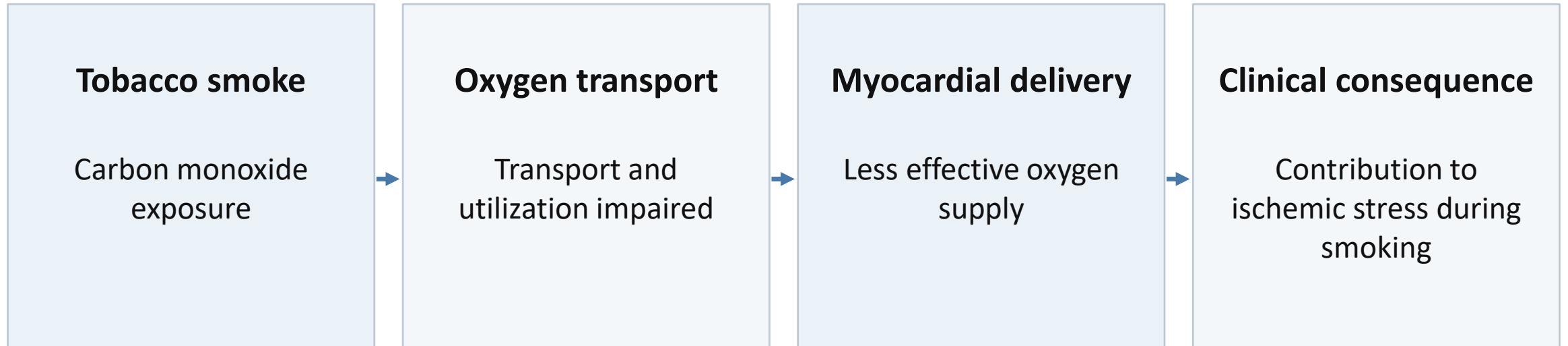


Conceptual pathway · editable schematic

Nicotine also creates fetal risk

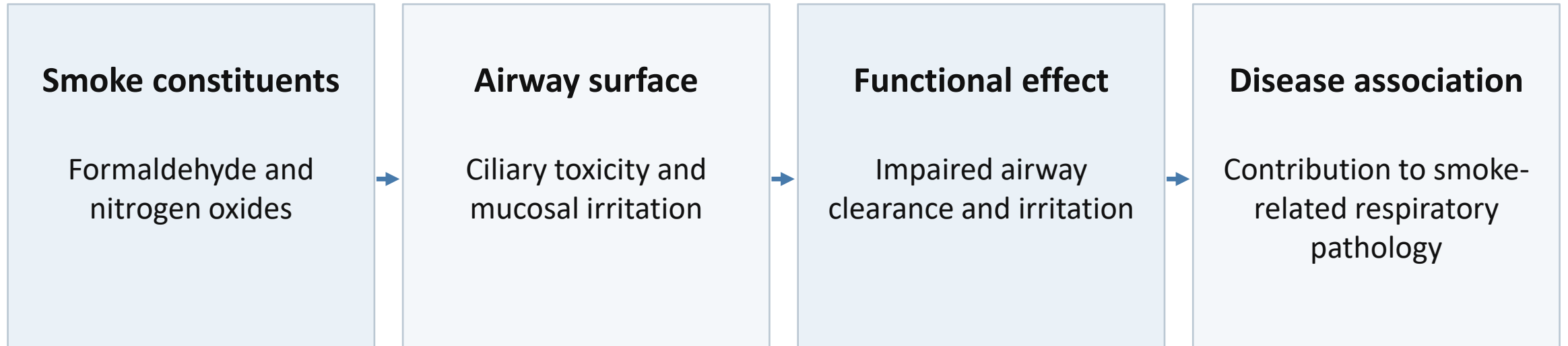
- Nicotine exposure during pregnancy may harm fetal brain development.
- The source links prenatal nicotine exposure to increased risk of preterm birth and stillbirth.
- These outcomes are not explained solely by adult respiratory disease.
- Fetal exposure is an additional reason tobacco injury is multisystem.

Carbon monoxide compromises oxygen availability



Conceptual pathway · editable schematic

Ciliary toxicants disrupt airway defense

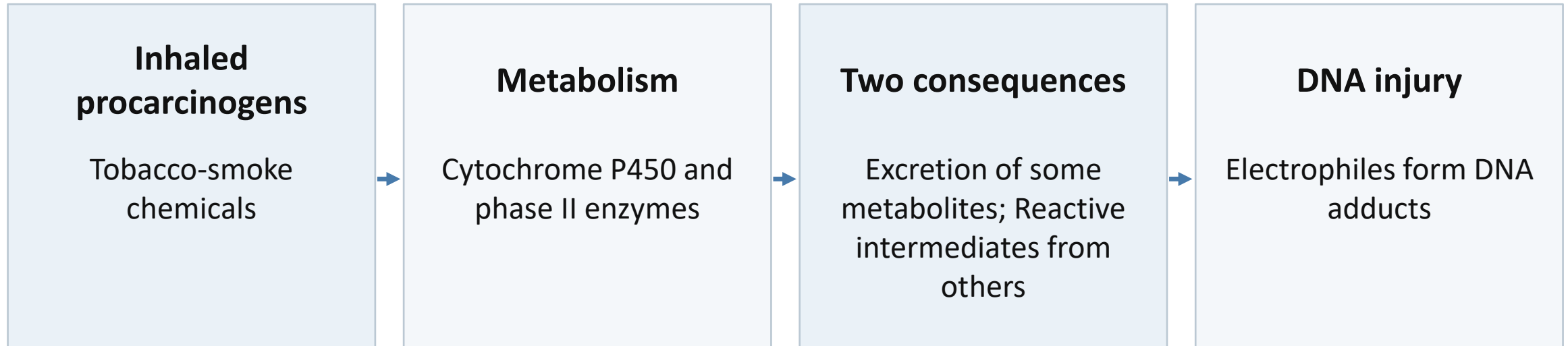


Conceptual pathway · editable schematic

Tobacco smoke is a leading exogenous carcinogen

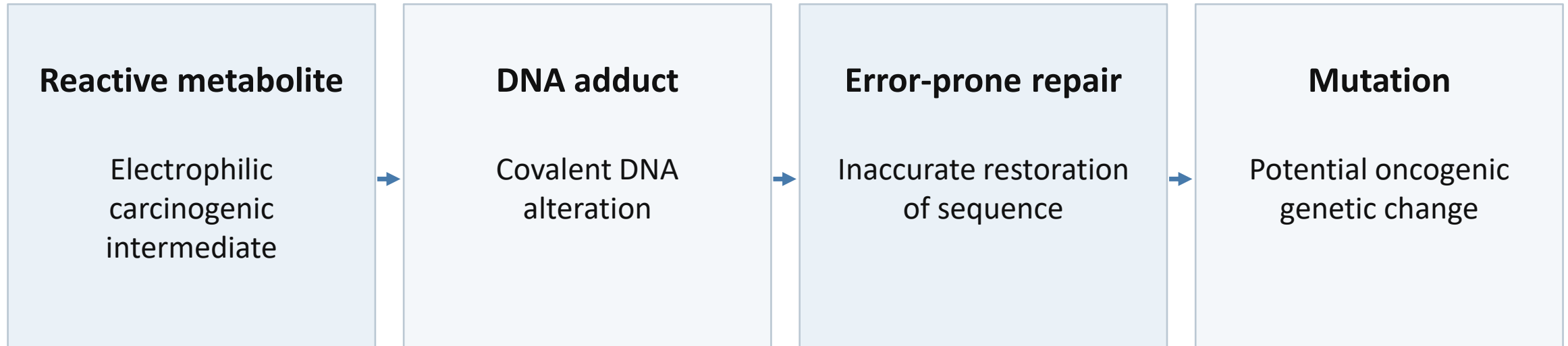
- Tobacco as the leading exogenous cause of human cancers.
- Smoking accounts for a large fraction of lung carcinomas account.
- Carcinogenic constituents act through exposure, metabolic activation, and DNA injury.
- Organ susceptibility varies with site of contact and distribution of carcinogens.

Tobacco carcinogens require metabolic interpretation



Conceptual pathway · editable schematic

DNA adducts create a route to oncogenic mutation



Conceptual pathway · editable schematic

Smoking-related lung cancers show mutational burden

- The neighboring Robbins section describes thousands of mutations in sequenced lung cancers from smokers.
- Mutational patterns resemble those generated experimentally by tobacco-smoke carcinogens.
- This supports a mechanistic link between chemical exposure and cancer genomes.
- Tumor genome alterations are evidence of prior injury, not a measure of pack-years by themselves.

Polycyclic aromatic hydrocarbons are carcinogenic

Chemical group

Polycyclic aromatic hydrocarbons;
Benzo[a]pyrene is an example

Pathologic action

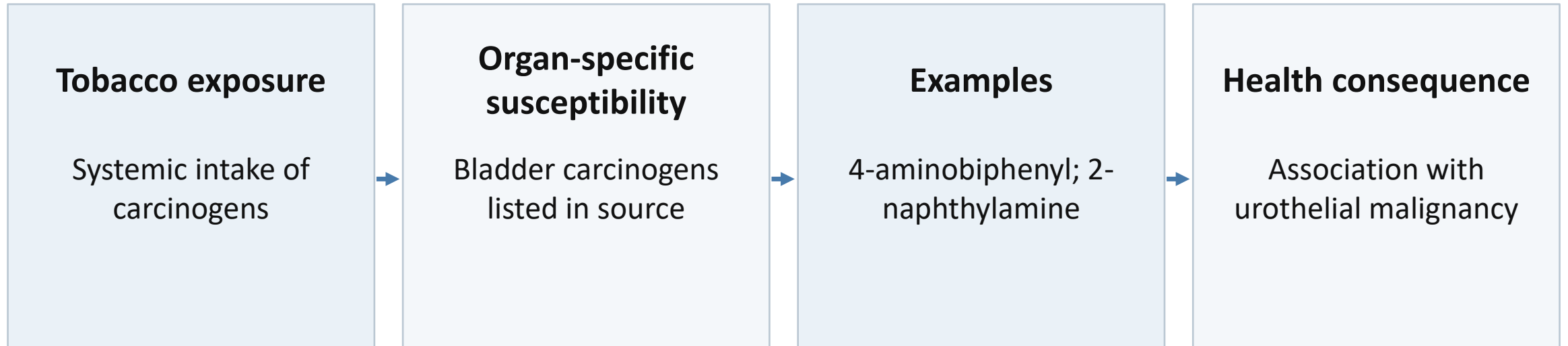
Metabolism can produce DNA-damaging
intermediates and mutagenic lesions

Airway exposure and systemic distribution help explain cancer at multiple sites.

Tobacco-specific nitrosamines are organ-relevant

Organ or site	Carcinogens listed in Robbins
Lung and larynx	Polycyclic aromatic hydrocarbons; NNK; polonium-210
Esophagus	NNN
Pancreas	NNK
Oral cavity	NNK; NNN; additional agents depending on exposure

Bladder cancer illustrates exposure beyond the lung



Conceptual pathway · editable schematic

Tobacco-linked cancers involve multiple organs

Site category	Examples listed by Robbins
Respiratory and upper aerodigestive	Lung, larynx, oral cavity, esophagus
Digestive and hepatopancreatic	Pancreas, liver, colon
Genitourinary / reproductive	Bladder, kidney, cervix
Hematopoietic	Hematopoietic malignancies

Tobacco interacts with additional carcinogens

Asbestos / uranium exposure

Smoking greatly increases lung carcinoma incidence in exposed workers

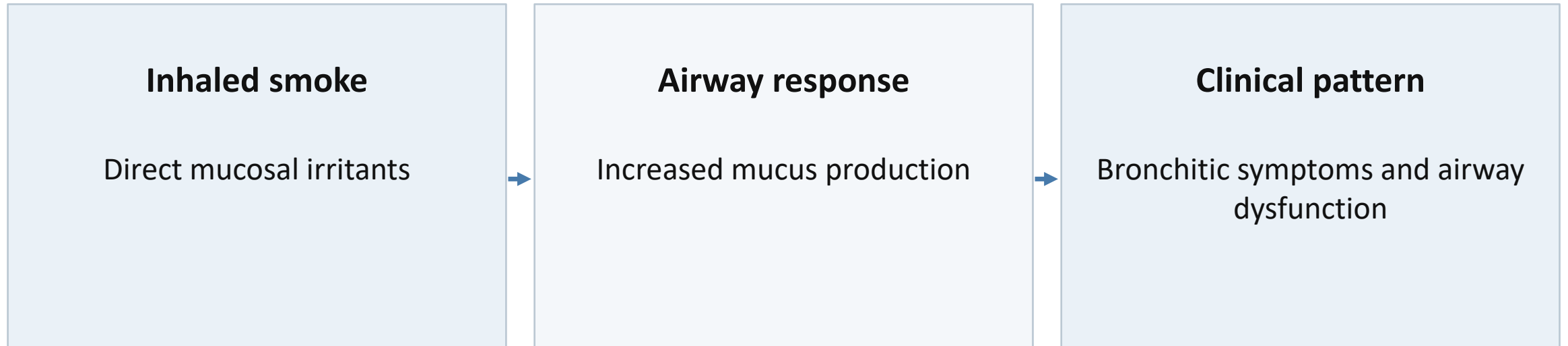
Alcohol consumption

Combined tobacco and alcohol exposure influences oral and laryngeal cancers

Cancer risk rises with cigarette exposure

- Robbins relates lung cancer risk strongly to the amount smoked and cumulative pack-years.
- The source figure illustrates increasing relative risk as cigarettes smoked per day increase.
- Avoid converting the figure into an invented smooth curve or extrapolated numerical estimates.
- Clinical exposure histories should capture dose, duration, and cessation.

Smoke directly irritates the tracheobronchial mucosa



Conceptual pathway · editable schematic

Smoke-related bronchitis involves mucus and injury

Airway response

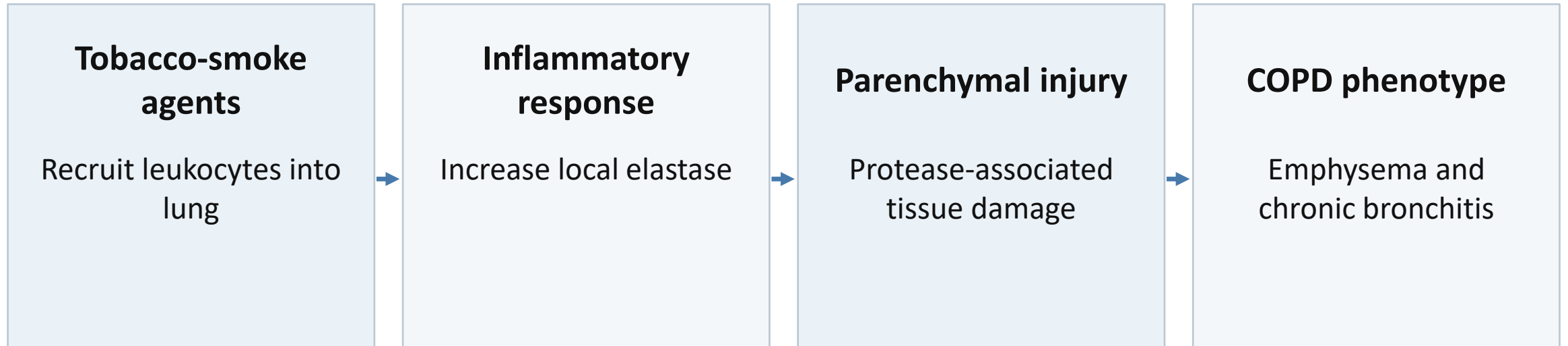
Mucosal irritation with increased mucus secretion

Functional impact

Symptomatic airway obstruction and impaired clearance

Mucus production is a tissue response; It does not itself establish a cancer diagnosis.

Inflammatory proteases contribute to COPD



Conceptual pathway · editable schematic

Emphysema and chronic bronchitis are distinct

Emphysema

Smoke-induced inflammation and protease-associated injury

Destruction component of COPD

Chronic bronchitis

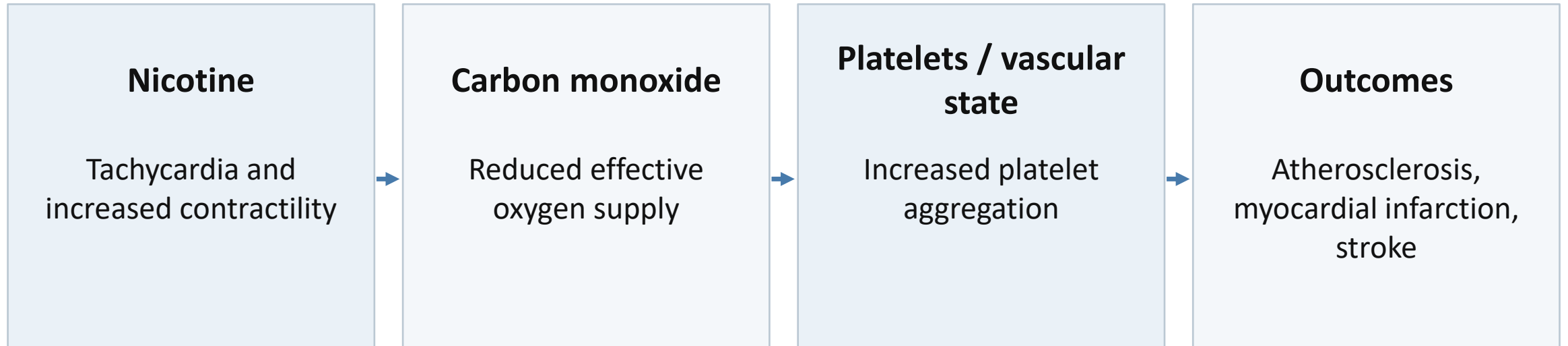
Airway irritation and increased mucus production

Airway-predominant component of COPD

Tobacco exacerbates other pulmonary conditions

- Smoking exacerbates asthma in the Robbins source.
- It is associated with increased risk for pulmonary tuberculosis.
- These harms occur in addition to chronic bronchitis, emphysema, and cancer.
- A respiratory differential should consider multiple smoking-associated diagnoses.

Cardiovascular toxicity has multiple pathways



Conceptual pathway · editable schematic

Smoking worsens the oxygen supply–demand balance

Oxygen supply falls

Carbon monoxide-related hypoxia; Coexisting lung disease

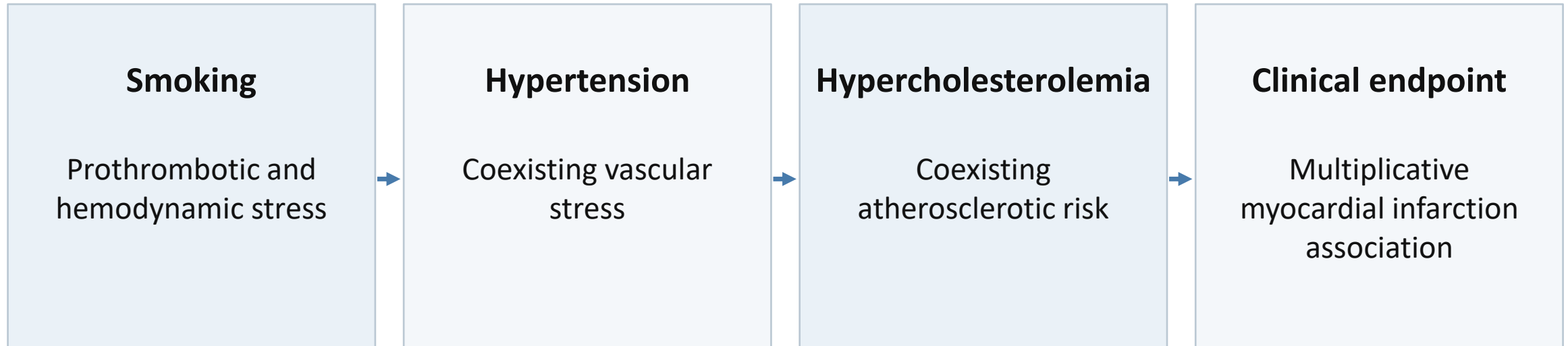
Oxygen demand rises

Nicotine-associated increased rate, contractility, and output

Smoking modifies acute coronary risk

- Increased platelet aggregation contributes to cardiovascular disease.
- Oxygen supply–demand mismatch compounds ischemic risk.
- Robbins also cites a decreased threshold for ventricular fibrillation.
- Atherosclerotic complications include myocardial infarction and stroke.

Other vascular risk factors amplify smoking harm



Conceptual pathway · editable schematic

Maternal smoking has multiple fetal consequences

Pregnancy outcome	Association reported in Robbins
Pregnancy loss	Increased spontaneous abortion risk
Gestational timing	Increased preterm birth risk
Fetal growth	Intrauterine growth restriction
Additional hazard	Stillbirth and possible fetal brain developmental injury

Preconception cessation matters for fetal growth



Conceptual time course · durations are not drawn to scale

Environmental smoke reproduces major disease risks

- Passive tobacco inhalation causes lung cancer in nonsmokers.
- Exposure is also associated with coronary atherosclerosis and fatal myocardial infarction.
- Second-hand smoke is therefore not merely an odor or nuisance.
- Smoke-free shared environments address disease risk among nonsmokers.

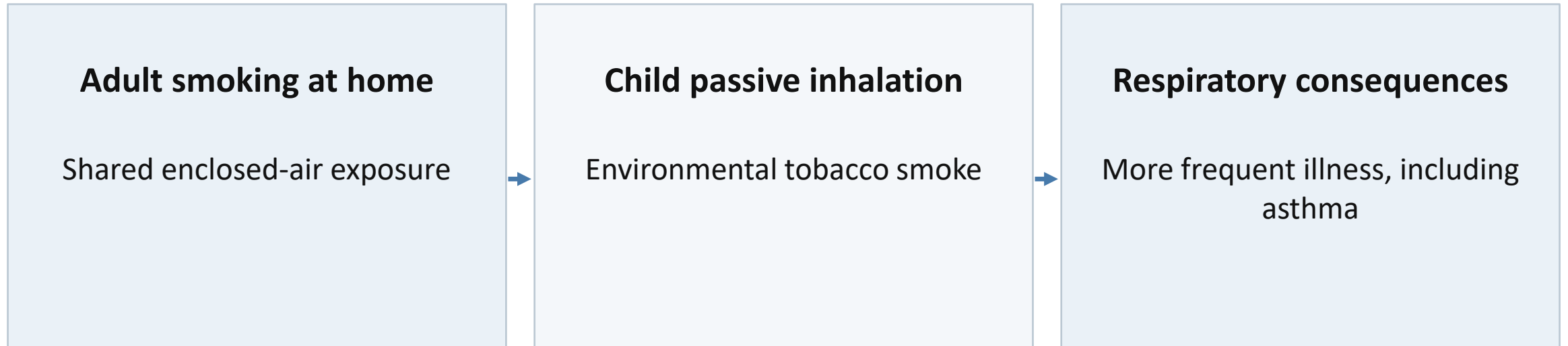
Lung cancer and passive exposure: Relative risk

$\approx 1.3\times$

Relative risk in exposed nonsmokers versus unexposed nonsmokers

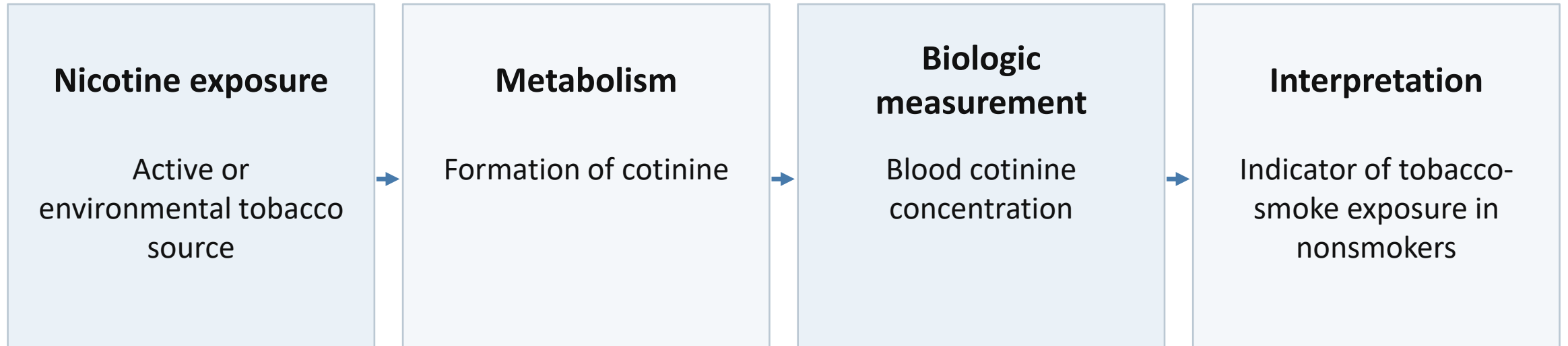
Source estimates · interpretation requires the population and period specified in the lecture notes

Children are particularly affected by home exposure



Conceptual pathway · editable schematic

Cotinine indicates absorbed nicotine exposure



Conceptual pathway · editable schematic

Smoke-free policies affect biologic exposure

- Median cotinine levels in US nonsmokers fell by more than 70% since about 2000.
- The text attributes this decline in part to nonsmoking policies in public places.
- Household exposure remains an important concern, especially for children.
- Population biomarker trends complement self-reported exposure histories.

Tobacco affects disorders beyond lung and heart

Disorder category	Associations listed in Robbins
Metabolic	Type 2 diabetes
Inflammatory	Rheumatoid arthritis
Ophthalmic	Age-related macular degeneration
Reproductive / sexual	Ectopic pregnancy; erectile dysfunction

Link each agent to a distinct injury mechanism

Agent / mixture	Predominant injury	Clinical connection
Nicotine	Nicotinic receptor/autonomic effects	Hemodynamic stress; dependence
CO	Impaired oxygen transport / utilization	Myocardial supply limitation
Irritant gases	Ciliary and mucosal toxicity	Bronchitic injury
Carcinogens	Reactive metabolites and DNA damage	Tobacco-associated cancers

Link major pathology to mechanism

Disease	Relevant pathogenic thread
Lung carcinoma	Carcinogen metabolism → DNA adducts → mutations
COPD	Airway irritation + leukocyte recruitment + proteases
Myocardial infarction	Platelets, oxygen mismatch, and vascular risk factors
Fetal growth restriction	Maternal tobacco exposure during pregnancy

Case: Interpreting a smoking history

A patient has smoked 1 pack daily for 25 years and now reports a persistent cough.

What exposure measure should be recorded, and what pathologic processes should be considered?

- 25 pack-years of cumulative exposure.
- Airway mucosal irritation with increased mucus; Possible chronic lung disease.
- The history is also relevant to lung cancer and cardiovascular risk.

Case: Smokeless tobacco and an oral lesion

A patient who has never smoked cigarettes regularly uses chewing tobacco and develops a persistent oral mucosal lesion.

Why is the absence of cigarette smoking not reassuring?

- Smokeless tobacco is independently harmful.
- It is an important cause of oral cancer.
- Clinical evaluation of the lesion should not be dismissed based on smoking status.

Case: Myocardial ischemia in a smoker

A patient who smokes has hypertension and hypercholesterolemia and presents with ischemic chest discomfort.

Which tobacco-related mechanisms may act together?

- Nicotine-associated increased myocardial demand.
- Carbon monoxide-related oxygen supply limitation.
- Increased platelet aggregation and multiplicative risk-factor interaction.

Case: A nonsmoker with household exposure

A nonsmoker shares a home with a regular smoker. A child in the household has recurrent asthma symptoms.

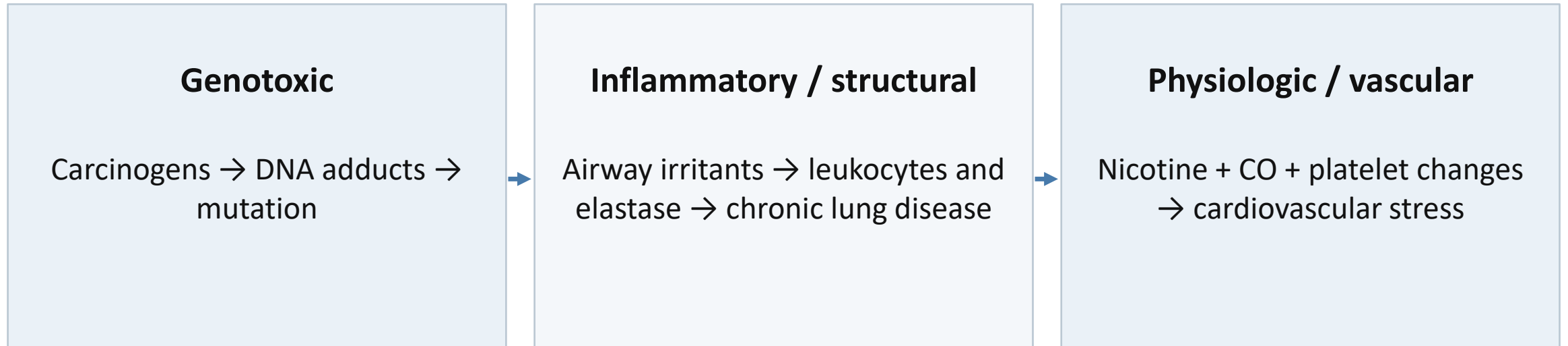
Which risks and exposure assessment are relevant?

- Second-hand smoke carries lung cancer, cardiovascular, and childhood respiratory risks.
- Blood cotinine can serve as a marker of absorbed nicotine exposure.
- Reducing home smoke exposure addresses a preventable environmental hazard.

Interpreting textbook risk estimates carefully

- The population figures and relative risks are reported estimates 11th edition.
- Mechanistic diagrams show causal concepts; They are not experimental plots.
- A reported association is not automatically an individual diagnostic criterion.
- Population-level associations are not individual deterministic forecasts.

Three mechanism families explain most damage



Conceptual pathway · editable schematic

Clinical synthesis: Tobacco is not a single-organ risk

- Assess route, dose, duration, and cessation status.
- Consider cancer, obstructive lung disease, vascular events, and reproductive effects.
- Remember indirect harm to nonsmokers, especially children and household contacts.
- Cessation lowers risk, but long-term malignancy risk does not disappear immediately.

References and provenance

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).

Chapter 9: Environmental and Nutritional Diseases.

Sections: Effects of Tobacco; Smoking and Lung Cancer; Smoking and Other Diseases.