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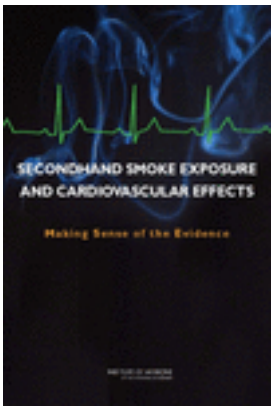

Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence

Committee on Secondhand Smoke Exposure and Acute Coronary Events; Institute of Medicine

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Data suggests that exposure to secondhand smoke can result in heart disease in nonsmoking adults. Recently, progress has been made in reducing involuntary exposure to secondhand smoke through legislation banning smoking in workplaces, restaurants, and other public places. The effect of legislation to ban smoking and its effects on the cardiovascular health of nonsmoking adults, however, remains a question.

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SUMMARY

Secondhand smoke, also known as environmental tobacco smoke, is a complex mixture made up of particles and gases and includes smoke from burning cigarettes, cigars, and pipe tobacco (sidestream smoke) and exhaled mainstream smoke. This includes aged smoke that lingers after smoking ceases. Data suggest that exposure to secondhand smoke can result in heart disease in nonsmoking adults. Progress has been made recently in reducing involuntary exposure to secondhand smoke in workplaces, restaurants, and other public places in the United States and abroad, often through legislation that bans smoking. The effect of legislation to ban smoking in public places and workplaces on cardiovascular health of nonsmoking adults, however, remains a question.

CHARGE TO THE COMMITTEE

The Centers for Disease Control and Prevention (CDC) asked the Institute of Medicine (IOM) to convene an expert committee to assess the state of the science on the relationship between secondhand-smoke exposure and acute coronary events. This report addresses that charge. Specifically, the committee reviewed available scientific literature on secondhand-smoke exposure (including short-term exposure) and acute coronary events and characterized the state of the science on the topic with emphasis on the evidence of causality and knowledge gaps that future research should address. The committee was asked to address the following group of questions presented in Box S-1.

BOX S-1 Specific Questions to the Committee

> The Centers for Disease Control and Prevention requested that the IOM convene an expert committee to assess the state of the science on the relationship between secondhand smoke exposure and acute coronary events. Specifically, the committee was to review available scientific literature on secondhand smoke exposure (including short-term exposure) and acute coronary events, and produce a report characterizing the state of the science on the topic, with emphasis on the evidence for causality and knowledge gaps that future research should address.
>
> In conducting its work the committee was to address the following questions:
>
> 1. What is the current scientific consensus on the relationship between exposure to

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secondhand smoke and cardiovascular disease? What is the pathophysiology? What is the strength of the relationship?

2. Is there sufficient evidence to support the plausibility of a causal relation between secondhand smoke exposure and acute coronary events such as acute myocardial infarction and unstable angina? If yes, what is the pathophysiology? And what is the strength of the relationship?
3. Is it biologically plausible that a relatively brief (e.g., under 1 hour) secondhand smoke exposure incident could precipitate an acute coronary event? If yes, what is known or suspected about how this risk may vary based upon absence or presence (and extent) of preexisting coronary artery disease?
4. What is the strength of the evidence for a causal relationship between indoor smoking bans and decreased risk of acute myocardial infarction?
5. What is a reasonable latency period between a decrease in secondhand smoke exposure and a decrease in risk of an acute myocardial infarction for an individual? What is a reasonable latency period between a decrease in population secondhand smoke exposure and a measurable decrease in acute myocardial infarction rates for a population?
6. What are the strengths and weaknesses of published population-based studies on the risk of acute myocardial infarction following the institution of comprehensive indoor smoking bans? In light of published studies' strengths and weaknesses, how much confidence is warranted in reported effect size estimates?
7. What factors would be expected to influence the effect size? For example, population age distribution, baseline level of secondhand smoke protection among nonsmokers, and level of secondhand smoke protection provided by the smoke-free law.
8. What are the most critical research gaps that should be addressed to improve our understanding of the impact of indoor air policies on acute coronary events? What studies should be performed to address these gaps?

COMMITTEE'S APPROACH TO ITS CHARGE

In response to CDC's request, IOM convened an 11-member committee that included experts in secondhand-smoke exposure, the pharmacology and pathophysiology of secondhand smoke, clinical cardiology, epidemiology (including cardiovascular epidemiology), and statistics. The committee met three times, including two open information-gathering sessions at which the members heard from stakeholders and researchers, conducted an extensive literature search, and reviewed relevant publications. The committee reviewed both pathophysiologic and epidemiologic studies, and considered the findings of a 2006 report by the surgeon general of the US Public Health Service, The Health Consequences of Involuntary Exposure to Tobacco Smoke.

Inherent in the committee's charge was the evaluation of three sets of relationships:

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- The association between secondhand-smoke exposure and cardiovascular disease, especially coronary heart disease and not stroke (question 1).
- The association between secondhand-smoke exposure and acute coronary events (questions 2, 3, and 5).
- The association between smoking bans and acute coronary events (questions 4, 5, 6, 7, and 8).

The committee reviewed the epidemiologic, clinical, and experimental studies relevant to the pathophysiology of secondhand smoke and cardiovascular effects, including coronary heart disease and acute coronary events. The pathophysiologic data not only provide insight into the potential modes of action underlying any effects of secondhand smoke on the cardiovascular system but provide evidence on a causal relationship between secondhand smoke and adverse cardiovascular outcomes.

Eleven publications played a key role in the committee's evaluation of smoking bans and were a focus of the committee's deliberations. Those publications assessed the effects of smoking bans on acute coronary events in the following locations: three on overlapping regions of Italy after implementation of a national smoking ban; two on the effects of a smoking ban in the city of Pueblo, Colorado, one with 18 months and one with 3 years of followup; and one each on the effects of smoking bans in Helena, Montana; Monroe County, Indiana; Bowling Green, Ohio; New York state; Saskatoon, Canada; and Scotland. Those 11 studies are observational studies that examined changes in heart-attack rates after implementation of smoking bans, and were not designed to answer questions about all three of the associations listed above. Most of them did not measure individual exposures to secondhand smoke or the smoking status of individuals; they were designed to evaluate the association between smoking bans and heart attacks, not the effects of secondhand-smoke exposure. The studies of the smoking bans in Monroe County, Indiana, and Scotland, however, had data on smoking status and conducted analyses only in nonsmokers. Those two studies were designed to assess the association between secondhand-smoke exposure and heart attacks.

SECONDHAND-SMOKE EXPOSURE AND CORONARY HEART DISEASE

The results of both case–control and cohort studies carried out in multiple populations consistently indicate that exposure to secondhand smoke increases the risk of coronary heart disease by about 25–30%, with higher estimates in the few studies that had better quantitative assessment of exposure. Data from epidemiologic studies with quantitative exposure assessment and from animal studies demonstrate a dose–response relationship. The epidemiologic evidence indicates increased risks even at the lowest exposures and a steep initial rise in risk followed by a gradual increase with increasing exposure. The pathophysiology of coronary heart disease and results of human chamber studies and laboratory studies of the constituents of secondhand smoke make such a relationship biologically plausible. The pathophysiology through which cigarette-smoking and exposure to secondhand smoke induce cardiovascular disease is complex and probably involves multiple chemical agents inasmuch as secondhand smoke itself and a number of its components have been shown to exert chronic cardiovascular toxicity. The association is also consistent with known associations between particulate matter (PM), a major constituent of secondhand smoke, and coronary heart disease.

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On the basis of its review of the data, the committee concurs with the current scientific consensus in the 2006 surgeon general's report that "the evidence is sufficient to infer a causal relationship between exposure to secondhand smoke and increased risks of coronary heart disease morbidity and mortality among both men and women." Although the committee found strong evidence of an association between chronic secondhand-smoke exposure and coronary heart disease and the relative risks are consistent, the evidence that might be used to determine the magnitude of the association—that is, the number of cases of disease that are attributable to secondhand-smoke exposure—is not as strong. Furthermore, many other individual lifestyle, community, and societal factors that lead to coronary heart disease could influence the magnitude of the effect in studies. The committee therefore did not estimate the size of the effect or the attributable risk.

SECONDHAND-SMOKE EXPOSURE AND ACUTE CORONARY EVENTS

Two of the epidemiologic studies reviewed by the committee analyzed changes in the hospitalization rate for acute coronary events after the implementation of smoking bans. They reported only events in nonsmokers (Monroe, Indiana) or analyzed nonsmokers and smokers separately (Scotland). Those studies provided direct evidence related to secondhand-smoke exposure and acute coronary events. Both studies showed reductions in the relative risk of acute coronary events in nonsmokers with the decrease in secondhand-smoke exposure that occurred after implementation of smoking bans. Because of differences between the studies (for example, in population and population size and in analysis), they did not provide sufficient evidence of the magnitude of the decrease in relative risk. The effect seen after implementation of smoking bans is consistent with data from the INTERHEART study, a case–control study of 15,152 first cases of acute myocardial infarction (MI, or heart attack) in 262 centers in 52 countries. Exposure to secondhand smoke increased the risk of nonfatal acute MI in a graded manner, with adjusted odds ratios of 1.24 (95% confidence interval [CI], 1.17–1.32) and 1.62 (95% CI, 1.45–1.81) in those least exposed (1–7 hours of exposure per week) and those most exposed (at least 22 hours of exposure per week), respectively. In contrast, a study that used data from the Western New York Health Study collected from 1995 to 2001 found that secondhand-smoke exposure was not significantly associated with an increase in the risk of MI. That study, however, looked at lifetime cumulative exposure to secondhand smoke, which is a different exposure metric from what was used in the other studies and does not take into account how recent the exposure was.

The nine other key epidemiologic studies that looked at smoking bans provided indirect evidence of an association between secondhand-smoke exposure and acute coronary events. It is not possible to separate the effect of smoking bans in reducing exposure to secondhand smoke from their effect in reducing active smoking in those studies, because they did not have individual smoking status or secondhand-smoke exposure concentrations; however, monitoring studies of airborne tracers[1] and biomarkers[2] of exposure to secondhand smoke have demonstrated that exposure to secondhand smoke is dramatically reduced after the implementation of smoking bans. Thus, those studies provided indirect evidence that at least part

[1]Airborne measures of exposure, such as the unique tracer nicotine or the less specific tracer PM, can demonstrate the contribution of different sources or venues of an exposure but do not reflect the true dose.
[2]Biomarkers of exposure to tobacco smoke, such as serum and salivary cotinine concentrations, integrate all sources of exposure and inhalation rates, but because of a short half-life, they reflect only recent exposures.

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of the decrease in acute coronary events seen after implementation of smoking bans could be mediated by a decrease in exposure to secondhand smoke. It is not possible to determine the magnitude of the effect that is attributable to changes in nonsmokers compared with smokers. It should also be noted that although the studies have limitations related to their taking advantage of natural experiments, they did directly evaluate the effects of an intervention (smoking bans and concomitant activities) on a health outcome of interest (acute coronary events).

As in the case of longer-term cardiovascular effects, experimental data have demonstrated that an association between secondhand-smoke exposure and acute coronary events is biologically plausible. Experimental studies in humans, animals, and cell cultures have demonstrated short-term effects of secondhand smoke, its components (such as oxidants, PM, acrolein, polycyclic aromatic hydrocarbons, benzene, and metals), or both on the cardiovascular system. There is sufficient evidence from such studies to infer that acute exposure to secondhand smoke at concentrations relevant to population exposures induces endothelial dysfunction, increases thrombosis, and potentially affects plaque stability adversely. Those effects occur at magnitudes relevant to the pathogenesis of acute coronary events. Furthermore, indirect evidence obtained from studies of ambient PM supports the notion that exposure to the PM in secondhand smoke could trigger acute coronary events or induce arrhythymogenesis in vulnerable myocardium.

None of the studies had information on the duration or pattern of exposure of individuals to secondhand smoke. That is, there was no information on how long or how often individuals were exposed before or after implementation of smoking bans. For example, it is not known whether individuals were exposed to high concentrations sporadically for short periods, to low concentrations more consistently, or both. Without that information, the committee could not determine whether acute exposures were triggering acute coronary events, chronic exposures were causing chronic damage that eventually resulted in acute coronary events, or a combination of chronic damage and an acute-exposure trigger led to the increased risk of acute coronary events.

The combination of the evidence from the epidemiologic studies and the information from the experimental studies and studies of PM is sufficient to support an inference of a causal relationship between exposure to secondhand smoke and acute coronary events. Although data from experimental studies have indicated that cardiovascular effects are seen after very brief exposures (less than 1 hour), the data from most of the epidemiologic studies do not include the duration of exposures before smoking bans, so the committee could not estimate the length of exposure required to increase the risk of acute MI.

SMOKING BANS AND ACUTE CORONARY EVENTS

All 11 key epidemiologic studies are relevant and informative with respect to the questions posed to the committee, and overall they support an association between smoking bans and a decrease in the incidence of acute coronary events. They show remarkable consistency: all the studies showed decreases in the rate of heart attacks (acute MIs) after implementation of smoking bans. The decreases ranged from about 6% to 47%, depending on the study and the form of analysis. The consistency in the direction of change gave the committee confidence that smoking bans decrease the rate of heart attacks. It is important to note that contextual factors associated with a ban—such as public comment periods, information announcing the ban, notices

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about the impending changes, education and outreach efforts on the adverse health effects of secondhand smoke, and support for smoking-cessation programs—are difficult, if not impossible, to separate from the impact of the ban itself and could vary from ban to ban. Therefore, committee conclusions regarding the effects of bans refer to the combined effects of different types of legislation and those contextual factors.

The committee was unable to determine the magnitude of effect on the basis of the 11 studies, because of variability among and uncertainties within them. Characteristics of smoking bans vary greatly among the locations studied and must be taken into account in reviewing results of epidemiologic studies. Those characteristics include the venues covered by the bans (such as offices, other workplaces, restaurants, and bars) and compliance with and enforcement of the bans. Other differences or potential differences among the studies include the length of followup after implementation, population characteristics (such as underlying rates of acute coronary events and prevalence of other risk factors for acute coronary events, including diabetes and obesity) and size, secondhand-smoke exposure levels before and after implementation, pre-existing smoking bans or restrictions, smoking rates, and method of statistical analysis. The time between implementation of a ban and decreases in secondhand smoke and acute cardiovascular events cannot be determined from the studies, because of the variability among the studies and indeed the difficulty of determining the precise time of onset of a ban. On the basis of its review of the available experimental and epidemiologic literature, including relevant literature on air pollution and PM, the committee concludes that there is a causal relationship between smoking bans and decreases in acute coronary events.

RESPONSES TO SPECIFIC QUESTIONS TO THE COMMITTEE

The committee was tasked with responding to a number of specific questions. The questions and the committee's responses are presented below.

1. *What is the current scientific consensus on the relationship between exposure to secondhand smoke and cardiovascular disease? What is the pathophysiology? What is the strength of the relationship?*

On the basis of the available studies of chronic exposure to secondhand smoke and cardiovascular disease, the committee concludes that there is scientific consensus that there is a causal relationship between secondhand-smoke exposure and cardiovascular disease. The results of a number of meta-analyses of the epidemiologic studies showed increases of 25–30% in the risk of cardiovascular disease caused by various exposures. The studies include some that use serum cotinine concentration as a biomarker of exposure and show a dose-response relationship. The pathophysiologic data are consistent with that relationship, as are the data from studies of air pollution and PM. The data in support of the relationship are consistent, but the committee could not calculate a point estimate of the magnitude of the effect (that is, the effect size) given the variable strength of the relationship, differences among studies, poor assessment of secondhand-smoke exposure, and variation in concomitant underlying risk factors.

2. *Is there sufficient evidence to support the plausibility of a causal relation between secondhand smoke exposure and acute coronary events such as acute myocardial infarction and unstable angina? If yes, what is the pathophysiology? And what is the strength of the relationship?*

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The evidence reviewed by the committee is consistent with a causal relationship between secondhand-smoke exposure and acute coronary events, such as acute MI. It is unknown whether acute exposure, chronic exposure, or a combination of the two underlies the occurrence of acute coronary events, inasmuch as the duration or pattern of exposure in individuals is not known. The evidence includes the results of two key studies that have information on individual smoking status and that showed decreases in risks of acute coronary events in nonsmokers after implementation of a smoking ban. Those studies are supported by information from other smoking-ban studies (although these do not have information on individual smoking status, other exposure-assessment studies have demonstrated that secondhand-smoke exposure decreases after implementation of a smoking ban) and by the large body of literature on PM, especially $PM_{2.5}$, a constituent of secondhand smoke. The evidence is not yet comprehensive enough to determine a detailed mode of action for the relationship between secondhand- smoke exposure and a variety of intervening and pre-existing conditions in predisposing to cardiac events. However, experimental studies have shown effects that are consistent with pathogenic factors in acute coronary events. Although the committee has confidence in the evidence of an association between chronic secondhand-smoke exposure and acute coronary events, the evidence on the magnitude of the association is less convincing, so the committee did not estimate that magnitude (that is, the effect size).

3. *Is it biologically plausible that a relatively brief (e.g., under 1 hour) secondhand smoke exposure incident could precipitate an acute coronary event? If yes, what is known or suspected about how this risk may vary based upon absence or presence (and extent) of preexisting coronary artery disease?*

There is no direct evidence that a relatively brief exposure to secondhand smoke can precipitate an acute coronary event; few published studies have addressed that question. The circumstantial evidence of such a relationship, however, is compelling. The strongest evidence comes from air-pollution research, especially research on PM. Although the source of the PM can affect its toxicity, particle size in secondhand smoke is comparable with that in air pollution, and research has demonstrated a similarity between cardiovascular effects of PM and of secondhand smoke. Some studies have demonstrated rapid effects of brief secondhand-smoke exposure (for example, on platelet aggregation and endothelial function), but more research is necessary to delineate how secondhand smoke produces cardiovascular effects and the role of underlying pre-existing coronary arterial disease in determining susceptibility to the effects. Given the data on PM, especially those from time-series studies which indicate that a relatively brief exposure can precipitate an acute coronary event, and the fact that PM is a major component of secondhand smoke, the committee concludes that it is biologically plausible for a relatively brief exposure to secondhand smoke to precipitate an acute coronary event.

With respect to how the risk might vary in the presence or absence of pre-existing coronary arterial disease, it is generally assumed that acute coronary events are more likely to occur in people who have some level of pre-existing disease, although that underlying disease is often subclinical. There are not enough data on the presence of pre-existing coronary arterial disease in the populations studied to assess the extent to which the absence or presence of such pre-existing disease affects the cardiovascular risk posed by secondhand-smoke exposure.

4. *What is the strength of the evidence for a causal relationship between indoor smoking bans and decreased risk of acute myocardial infarction?*

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The key intervention studies that have evaluated the effects of indoor smoking bans consistently have shown a decreased risk of heart attack. Research has also indicated that secondhand-smoke exposure is causally related to heart attacks, that smoking bans decrease secondhand-smoke exposure, and that a relationship between secondhand-smoke exposure and acute coronary events is biologically plausible. All the relevant studies have shown an association in a direction consistent with a causal relationship (although the committee was unable to estimate the magnitude of the association), and the committee therefore concludes that the evidence is sufficient to infer a causal relationship.

5. *What is a reasonable latency period between a decrease in secondhand smoke exposure and a decrease in risk of an acute myocardial infarction for an individual? What is a reasonable latency period between a decrease in population secondhand smoke exposure and a measurable decrease in acute myocardial infarction rates for a population?*

No direct information is available on the time between a decrease in secondhand-smoke exposure and a decrease in the risk of a heart attack in an individual. Data on PM, however, have shown effects on the heart within 24 hours, and this supports a period of less than 24 hours. At the population level, results of the key intervention studies reviewed by the committee are for the most part consistent with a decrease in risk as early as a month following reductions in secondhand-smoke exposure; however, given the variability in the studies and the lack of data on the precise timing of interventions, the smoking-ban studies do not provide adequate information on the time it takes to see decreases in heart attacks.

6. *What are the strengths and weaknesses of published population-based studies on the risk of acute myocardial infarction following the institution of comprehensive indoor smoking bans? In light of published studies' strengths and weaknesses, how much confidence is warranted in reported effect size estimates?*

Some of the weaknesses of the published population-based studies of the risk of MI after implementation of smoking bans are

- Limitations associated with an open study population and, in some cases, with the use of a small sample.
- Concurrent interventions that reduce the observed effect of a smoking ban.
- Lack of exposure-assessment criteria and measurements.
- Lack of information collected on the time between the cessation of exposure to secondhand smoke and changes in disease rates.
- Differences between control and intervention groups.
- Nonexperimental design of studies (by necessity).
- Lack of assessment of the sensitivity of results to the assumptions made in the statistical analysis.

The different studies had different strengths and weaknesses in relation to the assessment of the effects of smoking bans. For example, the Scottish study had such strengths as prospective design and serum cotinine measurements. The Saskatoon study had the advantage of comprehensive hospital records, and the Monroe County study excluded smokers. The population-based studies of the risk of heart attack after the institution of comprehensive smoking bans were consistent in showing an association between the smoking bans and a decrease in the risk of acute coronary events, and this strengthened the committee’s confidence

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in the existence of the association. However, because of the weaknesses discussed above and the variability among the studies, the committee has little confidence in the magnitude of the effects and, therefore, thought it inappropriate to attempt to estimate an effect size from such disparate designs and measures.

7. *What factors would be expected to influence the effect size? For example, population age distribution, baseline level of secondhand smoke protection among nonsmokers, and level of secondhand smoke protection provided by the smoke-free law.*

A number of factors that vary among the key studies can influence effect size. Although some of the studies found different effects in different age groups, these were not consistently identified. One major factor is the size of the difference in secondhand-smoke exposure before and after implementation of a ban, which would vary and depends on: the magnitude of exposure before the ban, which is influenced by the baseline level of smoking and pre-existing smoking bans or restrictions; and the magnitude of exposure after implementation of the ban, which is influenced by the extent of the ban, enforcement of and compliance with the ban, changes in social norms of smoking behaviors, and remaining exposure in areas not covered by the ban (for example, in private vehicles and homes). The baseline rate of acute coronary events or cardiovascular disease could influence the effect size, as would the prevalence of other risk factors for acute coronary events, such as obesity, diabetes, and age.

8. *What are the most critical research gaps that should be addressed to improve our understanding of the impact of indoor air policies on acute coronary events? What studies should be performed to address these gaps?*

The committee identified the following gaps and research needs as those most critical for improving understanding of the effect of indoor-air policies on acute coronary events:

- The committee found a relative paucity of data on environmental cardiotoxicity of secondhand smoke compared with other disease end points related to secondhand smoke, such as carcinogenicity and reproductive toxicity. Research should develop standard definitions of cardiotoxic end points in pathophysiologic studies (for example, specific results on standard assays) and a classification system for cardiotoxic agents (similar to the International Agency for Research on Cancer classification of carcinogens). Established cardiotoxicity assays for environmental exposures and consistent definitions of adverse outcomes of such tests would improve investigations of the cardiotoxicity of secondhand smoke and its components and identify potential end points for the investigation of the effects of indoor-air policies on acute coronary events.
- The committee found a lack of a system for surveillance of the prevalence of cardiovascular disease and of the incidence of acute coronary events in the United States. Surveillance of incidence and prevalence trends would allow secular trends to be taken into account better and to be compared among different populations to establish the effects of indoor-air policies. Although some national databases and surveys include cardiovascular end points, a national database that tracks hospital admission rates and deaths from acute coronary events, similar to the SEER database for cancer, would improve epidemiologic studies.
- The committee found a lack of understanding of a mechanism that leads to plaque rupture and from that to an acute coronary event and of how secondhand smoke affects that process. Additional research is necessary to develop reliable biomarkers of early effects on plaque

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vulnerability to rupture and to improve the design of pathophysiologic studies of secondhand smoke that examine effects of exposure on plaque stability.

- All 11 key studies reviewed by the committee have strengths and limitations due to their study design, and none was designed to test the hypothesis that secondhand-smoke exposure causes cardiovascular disease or acute coronary events. Because of those limitations and the consequent variability in results, the committee did not have enough information to estimate the magnitude of the decrease in cardiovascular risk due to smoking bans or to a decrease in secondhand-smoke exposure. A large, well-designed study could permit estimation of the magnitude of the effect. An ideal study would be prospective; would have individual-level data on smoking status; would account for potential confounders, including other risk factors for cardiovascular events (such as obesity and age), would have biomarkers of mainstream and secondhand-smoke exposures (such as blood cotinine concentrations); and would have enough cases to allow separate analyses of smokers and nonsmokers or, ideally, stratification of cases by cotinine concentrations to examine the dose–response relationship. Such a study could be specifically designed for secondhand smoke or potentially could take advantage of existing cohort studies that might have data available or attainable for investigating secondhand-smoke exposure and its cardiovascular effects, such as was done with the INTERHEART study. Existing studies that could be explored to determine their utility and applicability to questions related to secondhand smoke include the Multi-Ethnic Study of Atherosclerosis (MESA) study, the American Cancer Society's CPS-3, the European Prospective Investigation of Cancer (EPIC), the Framingham Heart Study, and the Jackson Heart Study. Researchers should clearly articulate the assumptions used in their statistical models and include analysis of the sensitivity of results to model choice and assumptions.

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Making Sense of the Evidence

Committee on Secondhand Smoke Exposure and Acute Coronary Events

Board on Population Health and Public Health Practice

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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COMMITTEE ON SECONDHAND SMOKE EXPOSURE AND ACUTE CORONARY EVENTS

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REVIEWERS

This report has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's (NRC's) Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individual's for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Floyd E. Bloom, M.D.,** The Scripps Research Institute and **Rogene F. Henderson, Ph.D.,** Lovelace Respiratory Research Institute. Appointed by the National Research Council, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

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PREFACE

The untimely death of a family member, friend or coworker from acute cardiovascular events is a tragedy that repeats itself too many times each day. Overall age adjusted mortality rates for heart disease have fallen significantly since the 1950s. Yet heart disease is still the leading cause of death in the US. Ischemic heart disease killed nearly 424,900 people in the US in 2006; or around half of the heart attacks that occurred that year.

Largely we have been focused on prevention of ischemic heart disease at the individual level, through identification of genetic risk factors and modification of lifestyle factors like diet and physical fitness. Chief among these has been smoking and the role that it has played both in chronic and acute cardiac diseases.

More recently we have begun to appreciate that the environment plays a role. Years of careful research have elucidated a role for fine particulate air pollution formed from the combustion of fossil fuels in premature mortality due to cardiac disease. As smoking bans were put in place a number of researchers observed that there were reductions in hospital admissions and deaths due to acute cardiovascular events.

In carrying out our research it became clear that, while we have learned much about why and how tobacco smoke, and particulate air pollution, aggravate cardiovascular disease, there is still much to learn. The paucity of information about cardiovascular toxicity of chemicals, even those in tobacco smoke, is indicative of the lack of attention that has been paid to environmental contributions to cardiovascular disease.

It is hoped that our report will spur efforts to learn more. Too many people die prematurely each year to do otherwise.

I am deeply appreciative of the expert work of our committee members: Neal Benowitz, Aruni Bhatnagar, Francesca Dominici, Steve Fienberg, Gary Friedman, Kathie Hammond, Jiang He, Suzanne Oparil, Eric Peterson, and Ed Trapido. This was an extraordinary group who each provided important contributions to the final report. It has been a privilege and a pleasure to work with the Institute of Medicine staff, study director Michelle Catlin and her excellent team Rita Deng and Raina Sharma, as well as Jennifer Saunders and Naoko Ishibe, Sc.D. Without them, this report would not have been possible. I thank those who provided expert presentations and background materials, and gave us much to think about: Captain Matthew McKenna, M.D., M.P.H. and Darwin Labarthe, M.D., M.P.H., Ph.D., the Centers for Disease Control and Prevention; Stanton Glantz, Ph.D., the University of California, San Francisco; Joel Kaufman, M.D., M.P.H., University of Washington, Seattle; Jon Samet, M.D., University of Southern California; Cynthia Hallett, American Nonsmokers' Rights Foundation; and Jared Jobe, Ph.D., National Heart, Lung and Blood Institute of the National Institutes of Health. In addition, I would like to thank individuals who assisted with the additional analyses of the committee:

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Aidan McDermott and Howard Chang, both from the Department of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University. And, last, but certainly not least, I am appreciative of the time and effort offered by our reviewers, Floyd E. Bloom (monitor), Rogene F. Henderson (coordinator), Scott Appleton, John C. Bailar III, Robert Brook, Stanton A. Glantz, Christopher B. Granger,. Arden Pope, Peter Rosen, Jonathan M. Samet, Michael Siegel, Ponisseril Somasundaran, and Noel S. Weiss.

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