



APPENDIX AVAILABLE ON REQUEST

Communication 15

Proceedings of an HEI Workshop on Further Research to Assess the Health Impacts of Actions Taken to Improve Air Quality

Health Effects Institute

Appendix C. Accountability Studies of Air Pollution and Human Health: Where Are We Now and Where Does the Research Go Next?

Correspondence may be addressed to Dr. Annemoon van Erp, Health Effects Institute, 101 Federal St. Suite 500, Boston, MA 02110

Although this document was produced with partial funding by the United States Environmental Protection Agency under Assistance Award CR-83234701 to the Health Effects Institute, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

This document did not undergo the HEI scientific editing and production process.

© 2010 Health Effects Institute, 101 Federal Street, Suite 500, Boston, MA 02110-1817

Appendix C

White Paper

Accountability Studies of Air Pollution and Human Health: Where Are We Now and Where Does the Research Go Next?

C. Arden Pope III, Ph.D.
Brigham Young University
Provo, UT

December 10, 2009

Prepared for the
Health Effects Institute Accountability Workshop
MIT Endicott House, Dedham, MA
December 17–18, 2009

Accountability studies, as discussed in this brief paper, are defined as studies that attempt to evaluate the impacts of specific actions taken to improve air quality. Obviously, one important aspect of accountability studies is to determine how quickly and how much the action actually reduced human exposures to air pollution. Certainly an exposure assessment component of any accountability study is critical. However, this paper will focus primarily on the epidemiologic considerations in evaluating human health impacts.

What are accountability studies?

Epidemiologic studies of air pollution are fundamentally attempts to exploit various dimensions of exposure variability in real-world settings. Most of these studies rely on naturally occurring exposure variability. Accountability studies are a subset of epidemiologic studies that attempt to exploit policy-related, planned, or controlled interventions that result in changes (usually reductions) in exposure and/or exposure variability. From a public policy perspective, accountability studies of policy-related planned interventions are important. Interest in these studies is motivated, in part, because these interventions may impose economic-related costs on society, and it is reasonable to

ask if there are compensating, tangible, and measurable improvements in air quality and public health.

Relationship with other common air pollution epidemiologic studies

From an epidemiologic standpoint, accountability studies are not easily characterized in contrast with or in relation to other epidemiologic study designs. One stylized way to compare accountability studies with other health studies of air pollution is provided in Table C.1. Studies of short-term episodes, daily time-series studies, and case-crossover studies exploit naturally occurring temporal variability from changes in weather conditions, emissions, etc. These studies have clearly demonstrated that short-term increases in exposure can result in increased cardiopulmonary mortality and morbidity, ischemic heart disease events, and other adverse health outcomes. These studies have also demonstrated that subsequent short-term reductions in exposure result in similar reductions in the same health outcomes, and they provide underlying estimates of improvements in health that could be expected from an intervention that results in short-term reductions in air pollution exposure.

Strictly ecologic cross-sectional studies, more sophisticated prospective cohort studies, and a few long-term longitudinal panel studies have primarily exploited long-term spatial variability. These studies have demonstrated that cross-sectional, long-term exposure to air pollution is associated with excess cardiopulmonary disease, lung cancer risk, deficits in lung function growth, and other adverse health endpoints — even while controlling for various important individual risk factors. Effects are estimated to be much larger than those due to only short-term exposure. These studies provide underlying estimates (or at least realistic priors) regarding health improvements that could be expected from a planned intervention that results in long-term reductions in air pollution exposures. In fact, studies by the EPA and others to make accountability estimates of the benefits of policy-related clean air actions are often based on these studies (U.S. EPA 1997; U.S. EPA 1999; U.S. OMB 2008).

Intervention studies

Also as noted in Table C.1, studies that have exploited changes in air pollution exposures to specific interventions have contributed to the epidemiologic evidence of adverse health effects of air pollution. Importantly, these studies have provided evidence regarding the potential health benefits from specific intervention-induced reductions in air pollution. Some of these studies are referred to as “natural” interventions studies. They are studies of specific but unplanned interventions (such as the intermittent operation of the steel mill in Utah Valley, the 1960’s copper strike, or the 1981–1982 U.S. economic recession that induced differential reductions in air pollution across the United States). Similar studies (often referred to as accountability studies) evaluate changes in exposure due to planned interventions (such as enforcement of new air quality standards, the Dublin coal ban, sulfur restrictions in fuel, etc.). The number of intervention studies (natural or planned) are currently fairly limited, but they are growing. They have provided additional evidence of adverse human health effects of air pollution and have added important and, in some cases,

unique additional evidence regarding time scales of exposure, especially regarding intermediate-term (months to years) time scales.

Ambiguities in classification of accountability studies

Many so-called accountability studies actually defy clear classification. For example, in Table C.1, the Harvard Six Cities study, as originally reported in 1993 (Dockery et al. 1993), is classified as a prospective cohort study that relied primarily on long-term spatial exposure variability. However, as originally designed, this study was intended to be a planned intervention (or accountability study). It was designed to study differential changes in air pollution across the six cities due to the implementation of the U.S. Clean Air Act, its amendments, and related national ambient air quality standards. An extended analysis of the Harvard Six Cities cohort (Laden et al. 2006) with a longer follow-up may be considered to be an accountability study because differential changes in air pollution eventually materialized. Both studies, however, are based on the same prospectively followed-up cohort and study design. Furthermore, after decades of follow-up, the differential changes in air pollution across the six cities were due only in part to the planned interventions associated with the Clean Air Act and enforcement of air quality standards. Economic factors (especially in the steel and coal industries) and other changes influenced air pollution levels. Even recent analyses of the American Cancer Society (ACS) cohort are attempts to evaluate the health benefits of the Clean Air Act (and other) related air quality improvements (Jerrett et al. 2007; Krewski et al. 2009) and could potentially be considered accountability studies.

Chay and Greenstone (2003a, 2003b) conducted two studies, one ostensibly an unplanned intervention or natural experiment (because it exploited economic-recession-induced changes in air pollution) and the other, ostensibly a planned intervention or accountability study (because it exploited Clean Air Act-related changes in air pollution). However, in both studies, differential exposures were due to a combination of the Clean Air Act, economic factors, and other factors. Similarly, the recent study of differential increases in life expectancy related to differential declines in air pollution between 1980 and 2000 (Pope et al. 2009) could be thought of and treated as an accountability study. Many of the changes in air pollution occurred at least partially as a result of Clean Air Act-related interventions. However, there were a variety of uncontrolled factors that influenced the changes in air pollution. Furthermore, this study was in important ways simply a classic natural experiment study with a straightforward first-differences analytic design.

Appeal and limitations of accountability studies

Although accountability studies often defy clear classification, the basic underlying approach is appealing. An ideal accountability study would be directly related to a specific, well-defined, and planned intervention. It would have a prospective design with adequate measurement of exposure and health endpoints before, during, and after the intervention. The intervention would result in temporally and/or spatially well-defined and clearly exogenous changes in exposure. A fundamental appeal of an ideal accountability study is that there is more exogeneity with regard to the changes in air pollution exposures and thus

less opportunity for confounding. This reasoning suggests that these planned intervention studies are the closest epidemiologic equivalent to controlled experimental studies (see Table C.1).

Accountability studies, however, are rarely or never ideal. They have limitations similar to other epidemiologic study designs. For example, there are often only very small changes in exposures, or larger changes are applicable only to small populations, resulting in limited statistical power. Exposure changes are often not truly exogenous, but are associated with other changes that may affect health, resulting in the potential of confounding. Also, the temporal changes in exposure are not always sharp, well-defined, or easily distinguished from natural temporal trends.

Importance and future of accountability studies

Recognizing some of the ambiguities and limitations of accountability studies does not diminish the quality or importance of some of these studies. There is clearly a future for planned intervention/accountability studies, and they are likely to eventually provide a block of epidemiologic evidence comparable to (and certainly overlapping with) evidence provided by time-series, case-crossover, prospective cohort, and other study designs. While we recognize that these studies have limitations similar to other epidemiologic studies, we should continue to be opportunistic with regard to exploring appropriate circumstances to conduct intervention studies (both natural and planned). How many other opportunities such as the Dublin coal ban (Clancy et al. 2002) are being missed? What more can we learn about the health effects of changes in air pollution that are continuing in the United States due to new air pollution standards? Are there opportunities in heavily polluted developing areas that have started — or may begin serious attempts — to control or reduce pollution? We can also attempt to be more innovative and proactive, similar to the example provided by the improved cooking stove study (McCracken et al. 2007). The Health Effects Institute's initiative and leadership regarding efforts to more fully exploit and even create opportunities for quality accountability research are important.

Intervention studies have added to and will continue to add to the epidemiologic evidence regarding the health effects of air pollution, and they will further improve our knowledge base. They provide direct evidence for specific interventions and help facilitate benefit–cost and related analyses of well-defined and planned policy actions. Accountability studies allow for better-planned prospective study design, data collection, and analysis. They also may have a clearer exogenous source of change in exposure with less potential for confounding. Ultimately, however, accountability, broadly defined and within the context of demonstrating compensating, tangible, and measurable improvements in air quality and public health, requires high-quality epidemiologic and related research that is also more broadly defined. This research must integrate exposure assessment efforts with a variety of epidemiologic and other study designs and approaches. Accountability studies can be, and are likely to be, an important part of this overall effort.

Table C.1. Outline of studies on the health effects of air pollution as related to accountability studies.

General Study Designs	Examples	Dimensions of Exposure Variability	What Have We Learned?
Episode	Smog in Donora, Penn., 1948 (Schrenk et al. 1949) Fog in London, U.K., 1952 (Logan 1953)	Short-term (a few days–weeks) temporal variability, from changes in weather conditions, emissions, and other.	Short-term increases in exposure result in increased cardiopulmonary mortality, morbidity, and other adverse health outcomes. Subsequent reduced exposure results in similar reductions in mortality and morbidity.
Time-series	NMMAPS (Samet et al. 2000) APHENA (Samoli et al. 2008)		
Case-crossover	Mortality in 27 cities (Franklin et al. 2007) Mortality in 14 cities (Schwartz 2004) Ischemic heart disease events (Pope et al. 2006)		
Cross-sectional	U.S. mortality (Lave and Seskin 1970; Özkaynak and Thurston 1987) Children’s health (Raizenne et al. 1996)	Primarily long-term (years–decades) spatial variability (with some longer-term temporal).	Annual mortality rates and children’s lung health correlate with long-term (years) cross-sectional differences in air pollution.
Prospective Cohort and long-term panel	Harvard Six Cities study (Dockery et al. 1993) American Cancer Society study (Pope et al. 2002) Women’s Health Initiative observational study (Miller et al. 2007) U.S. Medicare population study (Zeger		Excess cardiopulmonary disease and lung cancer risk, deficits in lung function growth, etc., associated with long-term exposure, even controlling for individual risk factors. Effects much larger than from short-term exposure.

	et al. 2008) Southern California Children’s Health Study (Gauderman et al. 2004)		
Unplanned intervention/ natural experiment	Utah Valley steel mill closure (Pope 1996) Recession (Chay and Greenstone 2003b) Copper strike (Pope et al. 2007)	Intervention-related changes in exposures. Includes short-term, long-term, and intermediate-term (few months–few years) temporal. Also, repeated cross-sectional, first difference, etc.	Adverse human health effects observed — comparable to other epidemiologic studies. These studies have added important additional evidence regarding time scales of exposure, especially regarding intermediate-term time scales.
Planned intervention/ accountability	Harvard Six Cities study (Laden et al. 2006) Clean Air Act (Chay and Greenstone 2003a) Dublin coal ban (Clancy et al. 2002) Hong Kong sulfur restrictions (Hedley et al. 2002) Chimney stove intervention (McCracken et al. 2007) U.S. life expectancy (Pope et al. 2009)		
Toxicology	Human instillation (Ghio and Devlin 2001) Human chamber controlled exposure (Brook et al. 2002; Brook et al. 2009) apoE mice inhalation (Sun et al. 2005)	Can include direct cross-subject variability for a variety of time scales.	Although not entirely consistent, the controlled experimental studies are providing growing complementary evidence of adverse human health effects of air pollution.

Abbreviations: APHENA = Air Pollution and Health; NNMAPS = National Morbidity, Mortality, and Air Pollution Study.

REFERENCES

- Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. 2002. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. *Circulation* 105:1534–1536.
- Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, Morishita M, Marsik FJ, Kamal AS, Kaciroti N, Harkema J, Corey P, Silverman F, Gold DR, Wellenius G, Mittleman MA, Rajagopalan S, Brook JR. 2009. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. *Hypertension* 54:659–667.
- Chay KY, Greenstone M. Air quality, infant mortality, and the Clean Air Act of 1970. October 2003a. NBER Working Paper No. W10053 (last updated 2/6/10). Available at Social Science Research Network: papers.ssrn.com/sol3/papers.cfm?abstract_id=461374. Accessed 7/2/10.
- Chay KY, Greenstone M. 2003b. The impact of air pollution on infant mortality: Evidence from geographic variation in pollution shocks induced by a recession. *Quart J Econ* 118:1121–1167.
- Clancy L, Goodman P, Sinclair H, Dockery DW. 2002. Effect of air-pollution control on death rates in Dublin, Ireland: An intervention study. *Lancet* 360:1210–1214.
- Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. 1993. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 329:1753–1759.
- Franklin M, Zeka A, Schwartz J. 2007. Association between PM_{2.5} and all-cause and specific-cause mortality in 27 US communities. *J Expo Sci Environ Epidemiol* 17:279–287.
- Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J. 2004. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med* 351:1057–1067.
- Ghio AJ, Devlin RB. 2001. Inflammatory lung injury after bronchial instillation of air pollution particles. *Am J Respir Crit Care Med* 164:704–708.
- Hedley AJ, Wong CM, Thach TQ, Ma S, Lam TH, Anderson HR. 2002. Cardiorespiratory and all-cause mortality after restrictions on sulphur content of fuel in Hong Kong: An intervention study. *Lancet* 360:1646–1652.
- Jerrett M, Newbold KB, Burnett RT, Thurston G, Lall R, Pope CA III, Ma R, De Luca P, Thun M, Calle J, Krewski D. 2007. Geographies of uncertainty in the health benefits of air quality improvements. *Stochastic Environmental Research and Risk Assessment* 21:511–522.
- Krewski D, Jerrett M, Burnett RT, Ma R, Hughes E, Shi Y, Turner MC, Pope CA III, Thurston G, Calle EE, Thun MJ. 2009. Extended Follow-Up and Spatial Analysis of the American

Cancer Society Study Linking Particulate Air Pollution and Mortality. HEI Research Report 140. Health Effects Institute, Boston, MA.

Laden F, Schwartz J, Speizer FE, Dockery DW. 2006. Reduction in fine particulate air pollution and mortality: Extended follow-up of the Harvard Six Cities Study. *Am J Respir Crit Care Med* 173:667–672.

Lave LB, Seskin EP. 1970. Air pollution and human health. *Science* 169:723–733.

Logan WP. 1953. Mortality in the London fog incident, 1952. *Lancet* 1:336–338.

McCracken JP, Smith KR, Díaz A, Mittleman MA, Schwartz J. 2007. Chimney stove intervention to reduce long-term wood smoke exposure lowers blood pressure among Guatemalan women. *Environ Health Perspect* 115:996–1001.

Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD. 2007. Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med* 356:447–458.

Özkaynak H, Thurston GD. 1987. Associations between 1980 U.S. mortality rates and alternative measures of airborne particle concentration. *Risk Anal* 7:449–461.

Pope CA III. 1996. Particulate pollution and health: A review of the Utah Valley experience. *J Expo Anal Environ Epidemiol* 6:23–34.

Pope CA III, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. 2002. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 287:1132–1141.

Pope CA III, Muhlestein JB, May HT, Renlund DG, Anderson JL, Horne BD. 2006. Ischemic heart disease events triggered by short-term exposure to fine particulate air pollution. *Circulation* 114:2443–2448.

Pope CA III, Rodermund DL, Gee MM. Mortality effects of a copper smelter strike and reduced ambient sulfate particulate matter air pollution. 2007. *Environ Health Perspect* 115:679–683.

Pope CA III, Ezzati M, Dockery D. 2009. Fine-particulate air pollution and life expectancy in the United States. *N Engl J Med* 360:376–386.

Raizenne M, Neas LM, Damokosh AI, Dockery DW, Spengler JD, Koutrakis P, Ware JH, Speizer FE. 1996. Health effects of acid aerosols on North American children: Pulmonary function. *Environ Health Perspect* 104:506–514.

Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. 2000. Fine particulate air pollution and mortality in 20 U.S. cities, 1987–1994. *N Engl J Med* 343:1742–1749.

Samoli E, Peng R, Ramsay T, Pipikou M, Touloumi G, Dominici F, Burnett R, Cohen A, Krewski D, Samet J, Katsouyanni K. 2008. Acute effects of ambient particulate matter on mortality in Europe and North America: Results from the APHENA study. *Environ Health Perspect* 116:1480–1486.

Schrenk HH, Heimann H, Clayton GD, Gafafer WM, Wexler H. 1949. Air Pollution in Donora, Pennsylvania: Epidemiology of the Unusual Smog Episode of October 1948. Bulletin 306. Washington, DC, Public Health Service.

Schwartz J. 2004. The effects of particulate air pollution on daily deaths: A multi-city case crossover analysis. *Occup Environ Med* 61:956–961.

Sun Q, Wang A, Jin X, Natanzon A, Duquaine D, Brook RD, Aguinaldo JG, Fayad ZA, Fuster V, Lippmann M, Chen LC, Rajagopalan S. 2005. Long-term air pollution exposure and acceleration of atherosclerosis and vascular inflammation in an animal model. *JAMA* 294:3003–3010.

U.S. Environmental Protection Agency. 1997. The Benefits and Costs of the Clean Air Act, 1970–1990. U.S. Environmental Protection Agency, Washington, DC. U.S. Environmental Protection Agency. 1999. The Benefits and Costs of the Clean Air Act, 1990–2010. U.S. Environmental Protection Agency, Washington, DC.

U.S. Office of Management and Budget. 2008. 2008 Report to Congress on the Benefits and Costs of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities. Office of Information and Regulatory Affairs, Washington, DC

Zeger SL, Dominici F, McDermott A, Samet JM. 2008. Mortality in the Medicare population and chronic exposure to fine particulate air pollution in urban centers (2000–2005). *Environ Health Perspect* 116:1614–1619.