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gOPINION

EDITORIAL COMMENT

Household Air Pollution and CVD

Identifying Best Directions for Research

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We face an increasing global burden of cardiovascular disease, principally due to a sharp rise in developing countries experiencing health transitions. Though it has long been known that hypertension, cigarette smoking, hypercholesterolemia, and diabetes are important cardiovascular risk factors, it is now increasingly appreciated that environmental factors such as fine-particulate air pollution represent a serious public health threat. As noted by Rajagopolan and Brook [1] in this issue, household air pollution from use of coal and biomass for cooking and space heating may well have a substantial, and potentially reversible, cardiovascular impact. Rajagopolan and Brook call for a concerted research program to estimate the impact and to develop and test interventions. They correctly note that there is a need to balance the cost of research with the necessity of additional information. Further, they identify 5 focus areas, including exposure assessment, biological mechanisms, epidemiology, candidate interventions, and cost-effectiveness. They argue that multidisciplinary teams are best equipped to tackle this complex issue from both scientific and societal perspectives.

Research, like many other goods and services, is a scarce resource for which we have to make difficult decisions about expected returns and opportunity costs. There is no question that properly done research offers substantive benefits at reasonable rates of return. Cutler and Kadiyala [2] analyzed the impact of research on cardiovascular health in the United States. They noted the dramatic decline in cardiovascular mortality seen over the last 50 years could be attributed to 3 major factors: high-technology care, low-technology care, and behavioral change. Quite remarkably, these declines have continued as age-adjusted death rates for coronary heart disease in the United States have declined from 187 deaths per 100,000 population in 2000 to 123 deaths per 100,000 in 2008 [3]. High-technology care includes coronary care units, cardiac surgery, and devices such as implantable defibrillators and circulatory support pumps. Low-technology care includes medical therapy for hypertension and hypercholesterolemia, as well as aspirin prophylaxis in appropriate patients. Behavioral changes include declines in cigarette smoking and changes in dietary fat intake. For identifying all 3 of these areas—high-technology care, low-technology care, and behavioral change—we can confidently say that biomedical research played a critical role. Were it not for biomedical research, coronary heart disease mortality rates might well be nearly 4× higher (405,000 of 1,579,000) in the United States [4]. Cutler and Kadiyala [2] estimated that the societal rate of return on biomedical research and cardiovascular disease is at least 4 to 1. Cardiovascular research, at least in high-income countries, has been an outstanding investment [5]. Given the large burden of cardiovascular disease in low- and middle-income countries, the persistent use of solid fuels globally, and the hypothesized cardiovascular effects of solid fuel smoke, we see a window of opportunity for research that could lead to positive impacts on public health practice and policy.

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PROSPECTIVE PLANNING

How can we ensure reasonable returns on the investment in biomedical research on the association between household air pollution and cardiovascular disease? What criteria should we use to rank priorities? How do we best leverage existing resources? How do we incorporate existing knowledge about the effects of ambient air pollution on blood pressure, myocardial ischemia, endothelial function, and inflammation? What proportion of resources should we dedicate toward fundamental and mechanistic, as opposed to applied research? Is it really necessary to elucidate mechanisms of disease when prior public health threats, such as smallpox and cholera, were largely conquered in the absence of such information? What proportion of resources should we dedicate toward implementation research versus the testing of new interventions? Should research funders primarily support large multidisciplinary groups, or focus on individual investigators working in relatively small laboratories or clinical research units? What proportion of a portfolio should go to funding “big science” projects? These are all difficult questions; questions that highlight substantial opportunity costs regardless of how reasoned our decisions are.

Research on the cardiovascular effects of household air pollution is by necessity of interest to multiple stakeholders, including researchers, policymakers, and implementers across the health, energy, and development sectors. There is increasing interest in developing systematic approaches to involve diverse stakeholder groups in the development and implementation of research priorities. For example, one group recently developed and piloted “a stakeholder informed approach” to prioritize comparative effectiveness research on genomic tests for cancer [6]. After performing a “landscape analysis” to identify candidate topics for research, the investigators sought to identify domains of high interest to diverse thought leaders and stakeholders, including patient advocacy groups, payers, manufacturers, leaders, policymakers, and community physicians. The investigators identified 9 critical domains, namely population impact, current standards of care, estimated strength of association, potential clinical benefits, potential harms, economic impacts, evidence of need, trial feasibility, and market factors. We might anticipate that these domains and others, like equity concerns, would be of variable interest to stakeholders in the cardiovascular impact of household air pollution. We might want to consider building on work like this to identify and engage key stakeholders and thereby prospectively identify our best criteria for research prioritization.

Within the sphere of clinical and population science, we need to make decisions about the relative importance of observational epidemiology, randomized trials, and novel program evaluation techniques that take advantage of natural experiments (Table 1). Observational epidemiology cohort studies can provide invaluable insights into candidate dose-response associations and possible confounders or mediators, whereas nested case-control studies built on existing cohorts can identify candidate biological pathways. Nonetheless, it is difficult to draw definitive conclusions from observational studies, given the potential impact of confounders such as climate, altitude, humidity, socioeconomic status, culture, diet, physical activity, and pollution from other sources. Randomized trials offer a high level of evidence unencumbered by unmeasured confounding, but also present substantial expense and logistical challenges (though prospective cohort studies also present complex logistical challenges). Today, only one completed randomized trial has assessed the health impacts of a chimney-stove intervention [7,8]. Natural experiments such as large-scale distribution of advanced biomass cook stoves with improved efficiency can take advantage of ongoing intervention programs and inform research by incorporating sophisticated analytical techniques in program evaluation. If properly done, analyses of natural experiments offer a cost-effective method for evaluating the potential public health impact of interventions. Nonetheless, a recent study illustrates the potential for significant bias in nonrandomized intervention studies due to limited controls for confounding influences of nonstove factors, particularly when assessing health benefits [9]. Another challenge is that technologies that reduce household air pollution will continue to evolve over time so that by the time an intervention has been tested it may have been replaced by a new innovation.

TEAM SCIENCE

It may seem intuitively obvious that research teams reflecting diverse, multidisciplinary backgrounds are more likely to be productive than individual investigators or small research groups are. Theoretical and empirical evidence supports the application of diverse, multidisciplinary approaches to problem solving. However, the benefits are often more

Table 1. Potential research examples

Research question	Proposed research and design
Association between HAP and CVD	Surveillance studies such as interrupted time series to measure the effect of large-scale interventions to reduce HAP on hard CV endpoints and surrogate measures (e.g., blood pressure) in multicountry, multiethnic, and at-risk groups. May be incorporated into existing cohorts.
Relationship between personal exposure level and CV risk and outcomes	Cohort studies taking into account other risk factors (e.g., tobacco smoking, climate, altitude). May be incorporated into existing cohorts.
Impact of HAP exposure on CV clinical outcomes including CVD death	Case-control studies. Acute effects of recent exposures (e.g., hours to days) and/or retrospective analysis of chronic effects using long-term exposure histories. Smaller samples possible.
Association between HAP and CV morbidity and mortality	Prospective long-term cohort studies including personal exposure levels and time course of exposure and CVD relationship.
Impact of new cook stoves or air filtration on CVD	RCT with sensitive CV risk surrogate markers (e.g., blood pressure) and, if feasible, hard CV outcomes. Best performed in multiple countries to capture regional differences in risk propensity and HAP exposure.

CV, cardiovascular; CVD, cardiovascular disease; HAP, household air pollution; RCT, randomized controlled trials.

modest than one might think, and even when present require certain pre-conditions. Diversity of approach works best when dealing with complex problems, when there is an ample supply of skilled problem solvers, and when there is sufficient diversity such that different groups of people will be able to leverage other groups' solutions [10]. As noted by Rajagopolan and Brook [1], these pre-conditions almost certainly exist in the case of cardiovascular disease and household air pollution. A particularly important challenge will be to promote involvement of in-country research collaborators, nongovernmental organizations, and policymakers.

ACCOUNTABILITY FOR DIRECTIONS CHOSEN

Once concerted research programs are underway, how and when do we evaluate their progress? "Results-based accountability" represents an approach by which governments and nonprofit funders evaluate the success or failure of their programs [11]. This approach has already been well tested for public health programs, such as a successful intervention to reduce teen pregnancy rates in Tillamook County, Oregon [12]. Briefly, we will need to prospectively identify "headline metrics" that are aligned with the goals and anticipated impact of any research programs we choose to fund. For basic science projects, we might choose to focus on publications in high-impact journals, citations, and innovative collaborations that lead to novel experiments. For applied projects, we might choose to focus on development of appropriate technological interventions that are ripe for clinical or community testing, as well as actual changes in intervention delivery, or public policy that lead to reduced pollution emissions and improved population cardiovascular health.

Once we have identified headline metrics, we track them and make forecasts about how they would be expected to behave were we to "continue business as usual." We then tell stories behind the trends and forecasts and use those stories to identify potentially valuable partnerships in changes in direction. A key point is that we do not use metrics to tell us what to do; instead, we use metrics as tools to help us identify best strategies.

CONCLUSIONS

Persistent household use of biomass and coal and growing cardiovascular disease burdens are major, and potentially connected, challenges facing

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governments, public health workers, research funders, and researchers. If we have learned anything from our experience in dealing with the American cardiovascular epidemic of the 20th century, it is that health research is absolutely essential to identify optimal solutions. Opportunities such as advanced biomass cook stoves developed over the past decade; low-cost, portable devices that enable us to measure intermediate cardiovascular disease endpoints in field-based settings (e.g., blood pressure, arterial function, heart rate variability); and new funding mechanisms such as the Clean Development Mechanism that facilitate large-scale intervention implementation were not possible in the past. To realize this potential, we will need to carefully consider criteria for prioritization, identify which circumstances and problems are best suited for large diverse teams to address, and implement rigorous ongoing self-evaluation based on the concepts of results-based accountability. In the case of advancing household air pollution research, investigators will need to coordinate study of social determinants and environment with classical measures of health science.

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