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The Conundrum of Cleaner Cookstove Interventions: Necessary but Insufficient?

Forty percent of the world's population, nearly 3 billion people, rely on biomass fuels for daily cooking and energy needs. Incomplete combustion of biomass fuels results in high exposures to household air pollution (HAP), a complex and toxic mixture. The most commonly measured pollutants include fine particulate matter ($PM_{2.5}$) and carbon monoxide (CO). In 2019, HAP was responsible for 2.3 million deaths and 91.5 million disability-adjusted life years (1). Together, cardiovascular disease and chronic respiratory diseases account for approximately 63% of all HAP-attributable deaths and 40% of disability-adjusted life years. Much of the burden is concentrated in low- and middle-income countries where, on average, an estimated 65% of households cook with solid fuels (2).

Despite this extraordinary burden of disease, randomized controlled trial (RCT) evidence supporting cleaner cookstove interventions to improve adult cardiopulmonary outcomes is lacking. Romieu and colleagues in 2009, and Hanna and colleagues in 2016, reported household-level chimney stove interventions versus traditional open-fire stoves, and intention-to-treat analyses found no effect on lung function decline, likely driven by low intervention uptake (3, 4). A report by Guarnieri and colleagues in 2015 similarly found no evidence that a household-level chimney stove intervention improved adult lung function, but separately published exposure-response analyses were suggestive of an effect (5, 6). Zhou and colleagues did conversely find that improved ventilation or biogas stoves for 9 years improved FEV_1 decline as compared with open fire, suggesting that a long duration of follow up may be required to see health effects (7). Although broader prospective cohorts, including work from our group, generally show a positive association between HAP exposure and blood pressure (BP) and, over the life course, cardiovascular mortality, data from RCTs is limited (8–10). For example, a secondary analysis of an ethanol intervention and a pre-/postimproved cookstove study suggests that interventions to reduce HAP exposure may improve diastolic or systolic BP, respectively (11, 12). Given these mixed results, the global health community continues to seek evidence in support of a cookstove intervention strategy to improve health.

In this issue of the *Journal*, Checkley and colleagues (pp. 1386–1397) examine the effect of a year-long, multifaceted liquefied petroleum gas (LPG) cookstove intervention as compared with biomass (commonly animal dung) cookstove on cardiopulmonary health in adults, specifically resting BP, peak expiratory flow (PEF), and respiratory symptoms as measured by the St. George's Respiratory Questionnaire (13). The intervention included provision of a three-burner LPG stove, education and behavioral messaging, and biweekly LPG fuel refills and stove inspections and repairs for the duration of the study. Repeated personal exposures to $PM_{2.5}$, black carbon, and CO exposures as well as kitchen area $PM_{2.5}$, CO, and, in a subset, nitrogen dioxide (NO_2) were measured. To understand patterns of stove use, temperature loggers were placed on LPG and biomass stoves in intervention homes and biomass stoves in control homes; 24 control homes also had temperature loggers placed on LPG stoves (71% of control households already owned an LPG stove). The authors are to be commended on the strength of their intervention, exposure measurement strategy, and objective health outcome assessments.

The primary finding of this impressive study was that a year-long LPG intervention with robust measures to enable LPG stove use was

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not associated with improvement in BP, PEF, or respiratory symptoms in women randomized to the cleaner burning LPG stove as compared with control. Strikingly, exposure-response analyses found no association between average personal $PM_{2.5}$ exposure and systolic or diastolic BP or postbronchodilator PEF (but did suggest that higher personal $PM_{2.5}$ exposure was associated with lower prebronchodilator PEF). These findings, like the many prior RCTs, once again leave us asking why cleaner cooking interventions do not appear to improve health. Given the deep literature linking air pollution exposure to cardiopulmonary risk, we posit that these results should not be construed as evidence that smoke from polluting cookstoves is safe. Instead, two factors may explain the results in this article.

First, the latency between HAP exposure and cardiopulmonary response may be too great for a year-long exposure reduction to induce a detectable difference (8). Enrolled women were, on average, 47.9 and 48.7 years old in the control and intervention arms, respectively, and these data suggest that established cardiopulmonary health trajectories are not altered by a short-term, later-life intervention. Although the ideal approach to HAP would be to eliminate polluting stoves and fuels in perpetuity, this is not yet feasible in most low- and middle-income countries. Given the many competing demands for scarce public health dollars (or soles), a limited-duration intervention to improve cardiopulmonary health may be more impactful if deployed earlier in life during sensitive windows of exposure (14, 15) compared with in later adulthood when these trajectories may already be set.

Second, despite the 98% exclusive LPG use in the intervention arm as defined by temperature loggers, high levels of exposure (on average, 30 $\mu g/m^3$ personal $PM_{2.5}$ exposure and 58 $\mu g/m^3$ kitchen area $PM_{2.5}$ concentration) were still observed postintervention, as was an overlapping distribution of personal $PM_{2.5}$ exposure with women randomized to control. In other words, exclusive use of the LPG intervention stove does not appear to have sufficiently reduced average exposures or produced a large enough exposure differential to impact health. Housing density and the number of intervention households per community are not provided, but randomization at the household level may have left intervention households exposed to pollution from neighboring households' cookstoves. As an extension of this, perhaps it is not just the average $PM_{2.5}$ exposure that is important but rather the peak exposures or the composition or mixture of pollutants that is particularly toxic. Checkley and colleagues have begun to examine this concept by measuring $PM_{2.5}$, black carbon, CO, and NO_2 exposures; banked filters and real-time exposure data should be leveraged to extend these analyses.

What is next for cleaner cookstoves research and policy? We offer three thoughts.

First, the fact that so many cookstove intervention trials register high exposures in intervention arms suggests that we must expand our focus beyond the household-level cookstove and endeavor to understand the totality of air pollution exposures in these communities. As these data suggest, a cleaner cookstove intervention alone may be insufficient to address this global public health crisis. Holistic air quality management approaches in low- and middle-income settings will entail both energy systems that deliver cleaner household energy at scale and at an affordable price and also coordinated efforts to reduce emissions from traffic, industry, and agriculture. In addition to directly improving health, many of these policies will reduce greenhouse gas emissions with global implications.

Second, this and other cleaner fuel trials throughout the Global South establish that even rural populations with limited prior exposure to modern fuels embrace cleaner cooking when it is convenient and cheap. This suggests that the central challenge going forward is to map out the regulatory and economic arrangements that will pave the way to societal transitions to cleaner household energy systems.

A final point pertains to research: as the list of cleaner cookstove RCTs accumulates, we see an opportunity to carry out pooled meta-analyses and leverage these studies' filter libraries and biospecimen repositories to better characterize the composition and mixture of HAP exposure and biomarkers of subclinical effect that may be more sensitive than outcomes examined in the primary intention-to-treat analyses. ■

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Lung Ultrasound in Early Preterm Life: A Window into the Future?

Because of the need for the lung to engage in gas exchange before alveolarization, preterm birth is fundamentally a developmental respiratory problem that often results in surfactant-deficient respiratory distress syndrome (RDS) and the need for assisted respiratory support (1). For many preterm infants, the interaction between abnormal lung development, altered lung mechanics, complications of respiratory support, and secondary factors creates a cascade of injury and inflammatory events, causing chronic lung disease, specifically bronchopulmonary dysplasia (BPD) (1). Reducing the burden of chronic lung disease has been hampered by difficulties in accurately identifying the lung conditions in early preterm life that predispose to later BPD. The study by Loi and colleagues in this issue of the *Journal* (pp. 1398–1409), verifying the potential of ultrasound of the lung (LUSS) to assess lung aeration and identify infants likely to progress to BPD, makes an important contribution to addressing this challenge (2).

In their multicenter, prospective, observational study, Loi and colleagues describe the relationship between standardized LUSS performed on Days 1, 7, 14, and 28 after birth with concurrent blood gas and clinical respiratory status in 147 preterm infants born at less than 31 weeks of gestation (2). Ultrasound interaction with the highly reflective pleura produces different artifact patterns that correlate with pulmonary aeration (3). The authors used a semiquantitative scoring system they had previously shown to predict short-term outcomes, including surfactant administration and response and noninvasive ventilation failure (2–5). Each lung was divided into three regions (upper anterior, lower anterior, and lateral), and scores were assigned on the basis of the observed ultrasound artifact pattern. Higher scores indicate worsening degrees of aeration. This LUSS score correlated moderately well with objective indices of impaired oxygenation and hypercapnia, and with subjective clinical assessment of RDS. The authors have highlighted key advantages of LUSS over other imaging modalities for this population. LUSS does not expose the preterm infant to ionizing radiation or require transfer from the neonatal ICU. Bedside ultrasound is widely available and accepted in neonatology. LUSS is easy to learn, and exhibits a high degree of interobserver agreement (3). The authors report that accurate image acquisition took an average of 3 minutes, although whether this can be replicated in less skilled hands requires confirmation.

BPD was diagnosed in 50% of infants in the study at 36 weeks corrected gestation. The most interesting finding of the study was the association between Days 7 and 14 gestational age–adjusted LUSS score and later BPD status. The ability of LUSS to predict BPD (71% sensitivity and 74% specificity at Day 7) is similar to existing BPD prediction tools (6–8). There is a strong rationale to focus on prediction in the first 2 weeks after preterm birth. In this period, the underdeveloped preterm lung with RDS is most at risk of injury (1, 9). It is increasingly apparent that the early events traditionally associated with BPD, such as oxygen exposure and barotrauma from invasive ventilation, are only part of the developmental, inflammatory, biotrauma, and mechanotrauma puzzle leading to BPD (10). This is also the period with the greatest potential to modulate BPD risk using interventions that blunt the early injury/inflammation cascade before secondary chronic injury occurs. The promising findings from Loi and colleagues' study suggest that serial LUSS offers a powerful functional tool for temporal characterization of early preterm lung disease.

Prediction is not prevention, and an ideal predictive tool should also guide intervention. There are many respiratory therapies available for RDS, but there is little evidence of difference between them with regard to BPD outcomes (1). The art of lung protection requires knowing therapy that may benefit a specific infant. As RDS is expressed differently within the lung and changes over time, optimizing respiratory therapies requires functional dynamic tools. Obtaining the fine balance between lung protection and injury has been hampered by crude tools, such as chest radiography, oxygenation, and clinical assessment. LUSS and electrical impedance tomography (EIT) are emerging dynamic, repeatable bedside methods of assessing lung function at a regional level that may offer the precision currently lacking (11, 12). As a research tool, EIT can differentiate ventilation homogeneity patterns related to molecular lung injury from respiratory interventions in preclinical

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