Randomized controlled trials (RCTs) are considered the “gold standard” study design in health research. The random allocation of participants to intervention and control groups minimizes systematic differences between groups and the biases that can result. RCTs have become standard practice in the evaluation of medical and pharmaceutical treatments. In contrast, environmental (and occupational) health research has relied primarily on observational methods; randomized studies to test the effect of an environmental exposure or the efficacy of an intervention to prevent or reduce exposure are rare.

A search of PubMed articles in journals focused on medicine, environmental health, and clinical trials revealed that only 0.6% of environmental health publications since 2000 were RCTs of an intervention to reduce exposure [S1 Text]. RCTs contribute a larger portion of the environmental health publications in top-ranked medical journals (4%) than in environmental health journals (0.4%)—an unsurprising result given the emphasis on clinical trials in medical research and the widespread perception that observational studies are inferior. The RCTs published to date have focused primarily on allergens, drinking water, household air pollution (HAP) from solid cooking fuels, lead, environmental tobacco smoke, and pesticides.

RCTs should be used more frequently to study environmental hazards (see Box 1). In calling for more randomized studies of interventions our objective is not to offer yet another admonishment of observational epidemiology [1–3]. The contributions that observational research has made to our understanding of environmental risks and the development of environmental health policy are impressive. Notable examples include ambient air pollution [4], lead [5], radon [6], arsenic [7], and asbestos [8], all of which are now known to cause substantial morbidity and mortality, and have policies in place to mitigate their health risks, based almost entirely on observational evidence [9]. Well-designed and carefully conducted randomized trials would complement this strong tradition of observational research. The fundamental advantages of randomized designs, such as minimization of confounding bias, are described elsewhere and need not be reiterated here. Instead, we aim to highlight how RCTs might be beneficial to environmental health research and describe some considerations for the appropriate use of RCTs to assess environmental risks and the efficacy of interventions.

Why Are More RCTs Needed?

Interventions to reduce or eliminate environmental exposures are urgently needed; environmental risks account for 13%–37% of the disease burden (quantified by disability-adjusted life years) in individual low- and middle-income countries [10,11]. The individual-level health risks of environmental exposures are often modest, but the population-level impacts are substantial because exposures are highly prevalent or ubiquitous and contribute to common diseases and disabilities [9]. Environmental exposures affect health in both high-income countries and low- and middle-income countries (LMIC), although the relative importance of specific risk factors and the magnitude of the risks vary with economic development [12].

RCTs can generally provide more definitive evidence of causality than observational studies. As a result, greater use of RCTs in environmental health would help to emphasize prevention over treatment by altering the perception that environmental risks are evaluated less rigorously than medical and pharmaceutical interventions. As previously noted in the context of HAP, the perception that environmental interventions are evaluated with insufficient rigor has important implications for the allocation of limited resources.

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Abbreviations: HAP, household air pollution; HEPA, high efficiency particulate air; LMIC, low- and middle-income countries; PM, particulate matter; RCT, randomized controlled trial; TSC, Total Sanitation Campaign; UGAR, Ulaanbaatar Gestation and Air Pollution Research.

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Provenance: Commissioned; externally peer reviewed
Improved cooking stoves is estimated at
Globally, the annual economic benefit of
outweigh costs by a ratio of 30 to 1 [16].
Air Act Amendments are projected to
cumulative benefits of the 1990 US Clean
in benefits of $17–$221 [15]. By 2020 the
hazards in the United States would result
each dollar invested to control lead
effective investments [14]. For example,
feasibly be studied using the RCT design.

health outcome and the timescale of the exposure–response relationship can
the intervention addresses a health risk affecting the local community; and (4) the
ethical issues—including clinical equipoise, the distribution of benefits and
risks, and the relevance of the intervention and health outcome to the study
population—must be carefully considered before conducting a randomized
controlled trial of an environmental intervention.

“[Randomized] studies would go a
long way in making the argument
about causality to health ministries
and international agencies that sup-
port them, who usually have very
limited resources to deal with a
number of large health problems.
They have the results of rigorous
studies focused on other means of
dealing with these same diseases…
At present, as the effectiveness and
cost of such measures has been
much better established, [HAP]
interventions garner little attraction.
On the other hand, the currently
available interventions are clearly
imperfect and will not serve to
to control the diseases” [13].

Environmental interventions are cost-
effective investments [14]. For example,
each dollar invested to control lead
hazards in the United States would result
in benefits of $17–$221 [15]. By 2020 the
cumulative benefits of the 1990 US Clean
Air Act Amendments are projected to
outweigh costs by a ratio of 30 to 1 [16].
Globally, the annual economic benefit of
halving the population without access to
improved cooking stoves is estimated at
$105 billion compared to a net cost of $34
billion [17].

Well-designed RCTs can also identify
inefficacious or even harmful interven-
tions. For example, several studies report-
ed that residential lead abatement in-
creased children’s blood lead levels,
which led to post-abatement lead-dust
standards to protect children from the
short-term risks of lead released during
abatement or renovation [18,19]. Even if
they do not increase health risks, non-
efficacious interventions can be a waste of
scarce resources and provide a false sense
of safety [20,21]. In the absence of
evidence, individuals will often turn to
unproven solutions—like surgical masks,
which are commonplace in many cities
with poor air quality but do little to reduce
health risks from air pollution [22].

Individuals Versus Populations

Most environmental health RCTs con-
ducted to date have evaluated interven-
tions on individuals or households, but
RCTs may also be appropriate for evalu-
ating interventions implemented at the
community level. For example, Patil and
colleagues conducted an RCT in 80
villages to evaluate the effect of India’s
Total Sanitation Campaign (TSC) on the
availability of improved sanitation, open
defecation behaviors, water quality, and
childhood diarrheal and gastrointestinal
illnesses [23]. Villages randomized to
the intervention group received the TSC,
while control group villages received the
TSC after the trial was completed. In
other situations, it may be infeasible (or
unethical) to randomize communities to
the intervention, and “natural experi-
ments” evaluating temporal changes in
exposure and health may be a more
appropriate design [24–27].

From a public health perspective, pro-
grams that reduce pollution emissions and
exposure among large populations will
always be preferable to interventions that
attempt to reduce exposure at the individ-
ual or household level after the pollutants
have been widely distributed. Neverthe-
less, RCT evaluations of interventions at
the individual or household level can have
tremendous value. Robust evidence that
exposure reductions lead to improvements
in health—even at the individual level—
may make the argument for policy inter-
ventions at the population level more
persuasive. The simplicity of the RCT
design also makes it relatively easy to
communicate results to non-researchers.
Thus, even if the intervention under study
is not feasible on a large scale, the
information generated on exposure–health
relationships may have relevance to pop-
ulation health and policy. Using RCTs to
demonstrate efficacy for individual- or
household-level interventions can also be
valuable if emissions or production cannot
be directly controlled. For example, wild-
fire smoke and radon are naturally occur-
ring pollutants for which risk management
involves exposure reduction primarily at
the household level [28,29].

RCTs are ideal for demonstrating
efficacy (performance of the intervention
under optimal conditions) but are gener-
ally inadequate for evaluating effectiveness
(performance of the intervention under
“real world” conditions) [30]. In clinical
trials external validity is often limited
because the demographics and health of
study populations differ from their target
populations [31]. External validity for
RCTs in environmental health can be
further influenced by the complexity of
“scaling-up” interventions to a larger
population [32]. An intervention’s impact
on health at the population level depends
on efficacy, but also on user compliance,
delivery, programming, and government
policy [33]. Thus, RCTs generally repre-
sent the first step in developing an effective
environmental intervention program.

Box 1. Randomized Controlled Trials

The RCT is a powerful research design that may have applicability to a wide range
of risk factors in the physical, built, and social environments. RCTs may be
appropriate and should be considered when the following criteria are met: (1)
there is uncertainty about which (if any) intervention is most effective (i.e., clinical
equipoise) or the gold standard intervention is not being implemented; (2) the
intervention to be studied is feasible and affordable to the local community; (3)
the intervention addresses a health risk affecting the local community; and (4)
the health outcome and the timescale of the exposure–response relationship can
feasibly be studied using the RCT design.
Some have suggested that the relatively small study populations in RCTs are only capable of detecting “large” health effects and that RCTs are therefore not useful in public (or environmental) health research [34]. However, this is not necessarily the case because the small populations in RCTs are offset by three advantages. First, the smaller populations in RCTs often allow for refined, individual-level exposure assessment using environmental measurements and/or exposure biomarkers that is often not possible in larger observational studies. A reduction of non-differential exposure misclassification can dramatically enhance our ability to detect relationships with health outcomes. Second, the ability to detect relationships between exposure and health depends, in part, on the size of the exposure gradient in the population. Ironically, it is the ubiquity of environmental exposures that makes their relationship with health difficult to uncover because “the hardest cause to identify is one that is universally present, for then it has no influence on the distribution of disease” [35]. RCTs can substantially increase the exposure gradient in the study population—and thus our ability to detect associations with health—by reducing exposure in the intervention group. Finally, environmental health researchers often struggle to identify the causative agent because many exposures share common sources and are therefore correlated. By reducing one specific exposure we can decrease its correlations with other exposures and more clearly identify the key agent(s) impacting health. For example, high efficiency particulate air (HEPA) filters reduce particulate matter (PM) air pollution concentrations indoors, but they have little effect on gaseous pollutants [36]. Thus, studies demonstrating health benefits from HEPA filtration provide evidence that PM plays an important role [36–38].

**Ethical Considerations**

RCTs raise important ethical questions, and while a comprehensive review of ethical considerations is beyond the scope of this essay, some issues with relevance to environmental health research should be mentioned. The fundamental question with all RCTs is whether it is ethical to intentionally increase exposure to environmental risks is greatest and where the risks are often concentrated at the household level [9,12]. These studies are ethical only if the intervention being tested is feasible and affordable in the local context and addresses a health risk of relevance to the population under study. Finally, researchers should clearly communicate that the study will not intentionally increase exposure to environmental hazards [47].

An important consideration for the RCT design is the timescale of the exposure-health relationship. It may be prohibitively expensive and difficult to mount RCTs for studying diseases with long latency periods, such as cancer or cardiovascular disease, but the RCT may be useful for testing the efficacy of interventions to reduce exposure to known carcinogens or cardiovascular risks (e.g., arsenic, lead) or for studying intermediate biological processes (e.g., systemic inflammation, endothelial dysfunction). The RCT design should also be considered in studies of acute or sub-chronic health effects and/or in situations with a well-defined exposure period of interest (e.g., pregnancy).

A key difference between clinical trials and RCTs of environmental interventions is that in the latter it is often difficult to blind participants and research personnel to intervention status. This may lead to biased effect estimates, particularly when investigating subjectively assessed health outcomes [48]. For example, unblinded studies of water treatment interventions in LMIC suggest that interventions produce substantial reductions in risk of diarrhea, while a smaller number of blinded studies have not found comparable benefits [49]. Even if participants cannot be blinded researchers should strive to rely on “hard,” objective outcomes, and personnel responsible for outcome assessment should be blinded (i.e., single blind).

Although many of the environmental health RCTs conducted to date have studied relatively simple interventions focused on a single environmental hazard, some have evaluated multifactorial interventions aimed at multiple exposures [50,51]. Other fields have applied the RCT design more frequently and ambitiously. For example, the “Moving to Opportunities” study randomized over 4,000 families in high-poverty areas of several US cities into one of two housing mobility intervention groups or a control group and evaluated relationships with a range of outcomes [52–56]. The MIT Poverty Action Lab is using RCTs to address a wide range of questions in international development [57].

Our ongoing Ulaanbaatar Gestation and Air Pollution Research (UGAAR) study provides a useful example of a RCT in environmental health. Several large, well-conducted observational studies have suggested a link between ambient air pollution and impaired fetal growth [58,59], but concerns about confounding and exposure misclassification remain [60]. We are randomizing approximately 500 pregnant women into either a HEPA filter intervention group or a control group (no filter); women in the intervention group will have HEPA filters operating in their home from enrollment until the child’s birth. Ulaanbaatar, Mongolia is an ideal location to test the efficacy of this intervention because it has extraordinarily high air pollution concentrations [61] that are likely to remain elevated for decades even under the most optimistic scenarios [62,63]. This situation is not unique—nearly 90% of the world’s population breathes air pollution that exceeds WHO guidelines, and concentrations are increasing in much of the world [64]—so there is value in identifying efficacious interventions that can reduce health risks in the near term until regulations, technology, and economic development can reduce air pollution to acceptable levels. The randomized design should minimize...
confounding, and the high pollution concentrations and large exposure gradients created by the intervention provide statistical power among a relatively small study population on which detailed, household-level exposure assessment can be conducted. HEPA filters are a feasible and affordable intervention, and impaired fetal growth is a relevant outcome in this population.

Conclusions

Randomized controlled trials are standard practice in clinical and pharmaceutical research but have not been embraced by environmental health researchers. Greater use of the RCT design would complement the tremendous contributions made by other methods—including both observational epidemiology and toxicology—to our understanding of environmental risks and the development of environmental health policy. Researchers, academic institutions, and funding agencies have a role to play in expanding the use of RCTs in environmental health research. Researchers should think creatively about potential interventions and consider the RCT as a possible study design to test their specific research question. Funding agencies should allocate money specifically for randomized studies of environmental interventions. In addition to its scientific advantages, this would provide the additional benefit of encouraging research that aims not only to identify problems but also to identify possible solutions. Ethical issues must be considered carefully, and while institutional ethics approval is necessary, it is not sufficient to ensure that the research is conducted ethically. The RCT design has important limitations and is not applicable to all research questions, so observational studies will, and should, remain the workhorse in environmental health research. Nevertheless, RCTs can help advance the field of environmental health by creating new knowledge of exposure–health relationships, providing more definitive evidence of causality, identifying efficacious interventions to reduce or eliminate exposure and health risks, and countering the perception that environmental risks are evaluated with inadequate rigor.

Supporting Information

S1 Text  Details of PubMed search for randomized controlled trials in environmental health. (DOCX)

Author Contributions

Wrote the first draft of the manuscript: RWA PKB BPL. Wrote the paper: RWA PKB BPL. ICMJE criteria for authorship read and met: RWA PKB BPL. Wrote the paper: RWA PKB BPL. The ICMJE criteria for authorship read and met: PKB BPL. Wrote the paper: RWA PKB BPL.

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Supporting Information

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Author Contributions

Wrote the first draft of the manuscript: RWA PKB BPL. Wrote the paper: RWA PKB BPL. ICMJE criteria for authorship read and met: RWA PKB BPL. Agree with manuscript results and conclusions: RWA PKB BPL.
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