REVIEW

Annals of Internal Medicine

Engineering Infection Controls to Reduce Indoor Transmission of Respiratory Infections

A Scoping Review

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Background: Engineering infection controls include a wide range of interventions used indoors to reduce occupants' exposure to respiratory pathogens.

Purpose: To identify and describe primary studies evaluating the effects of engineering infection control interventions designed to reduce the spread of respiratory infections transmitted through indoor air.

Data Sources: MEDLINE, Embase, Global Health, Cochrane Central Register of Controlled Trials, CINAHL, Scopus, and Environmental Science Collection from database inception to 12 December 2023.

Study Selection: English-language primary research articles evaluating engineering infection control interventions.

Data Extraction: Publication information, population characteristics, intervention details, and all relevant outcomes were abstracted by a reviewer and verified by a second, senior reviewer.

Data Synthesis: A total of 672 studies published between 1929 and 2024 were identified. Most (n = 606) evaluated environmental samples only, 57 included human participants, and 9 included sentinel animal subjects. About half of the studies included at least 1 intervention classified as pathogen inactivation (n = 405), with fewer involving pathogen removal (n = 200) or air exchange or dilution (n = 143). Across all studies, about half (n = 332) measured the quantity of viable nonpathogenic organisms from air samples, followed by the quantity of nonbiological particulates (n = 197) or viable pathogenic organisms (n = 149). Harms, such as toxic byproducts, were rarely measured.

Limitation: Exclusion of non–English-language publications and gray literature.

Conclusion: There is substantial heterogeneity in the available evidence. Gaps in evidence include studies measuring efficacy outcomes that are highly relevant for human infection transmission or harms. Refinements in classification of interventions and outcomes could strengthen reporting of these evaluations.

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Engineering infection controls use modifications to the physical environment or to equipment to reduce the risk for infection transmission indoors. They include a wide range of interventions, with some shown to reduce indoor transmission of respiratory infections among people, such as ventilation, portable air filtration, and germicidal ultraviolet (GUV) energy (1). The COVID-19 pandemic stimulated intense interest in such infection control practices, including investments in engineering controls and in studies to understand their effect (2–10).

Comprehensive evidence reviews are needed to better understand currently available indoor engineering infection controls and to identify gaps in evidence regarding their efficacy and safety. Recent reviews have focused on specific respiratory infections (such as COVID-19), particular workplaces (such as health care facilities), and mixed interventions (for example, ventilation and barriers) (2, 5–9, 11–17). No evidence synthesis thus far has comprehensively mapped evidence on all engineering infection control measures for all respiratory infections known to spread through indoor air.

Scoping reviews "map" the range, extent, and nature of research relevant to a broad question and can identify groups of studies that are suitable for systematic reviews (18). Given a lack of standardization in how engineering infection controls are defined, the wide range of outcomes that are of interest, and the variety of study designs used to assess their effects, a scoping review is an appropriate approach. This review seeks to clarify the key concepts related to studying health benefits

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and harms (if any) of engineering infection controls, compile key considerations for effectiveness of such interventions, examine how research is conducted on this topic, and identify gaps in knowledge. We identify and describe primary studies that evaluate the effects of engineering infection control interventions designed to reduce the spread of respiratory infections transmitted through indoor air.

METHODS

Our review was conducted and reported according to the Joanna Briggs Institute (18) methodology and the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) checklist (19). This activity was reviewed by the Centers for Disease Control and Prevention (CDC), was deemed to be research not involving human subjects, and was conducted in accordance with applicable federal law and CDC policy. Our protocol was registered on the Open Science Framework on 14 February 2024 (https://osf.io/5zmhd).

Eligibility Criteria

We developed a logic model, drawing input from team members with expertise in engineering methods, respiratory disease transmission, public health practice and policy, and evidence synthesis. This model conceptualizes the settings, study types, interventions, modifying factors, and outcomes within the scope of this review (**Supplement Figure 1**, available at Annals.org).

Supplement Table 1 (available at Annals.org) summarizes the inclusion and exclusion criteria for this review. We included research conducted in any country, in any enclosed setting (for example, transportation conveyances, health care facilities, schools, or experimental chambers), and of any analytical epidemiologic design. We excluded computational modeling studies without an eligible experimental component and studies that were purely descriptive without an evaluation of the effectiveness of the intervention. We included studies conducted in humans of any age, sex, race, or ethnicity as well as sentinel animal studies evaluating transmission of microorganisms that are pathogenic to humans. Studies evaluating animal-to-animal transmission of pathogens were excluded.

We developed a broad intervention classification system guided by prior schema (20, 21) and later modified based on multidisciplinary team feedback (**Supplement Table 2**, available at Annals.org). Briefly, we classified engineering infection control components into 2 broad categories: strategies that dilute or move air, and those that directly capture or inactivate pathogens. Within each strategy, the initial literature review identified a range of studied solutions and technologies, such as natural ventilation, dilution ventilation, laminar flow, photocatalytic oxidation, and GUV energy.

We categorized the reported study outcomes using a broad taxonomy developed for core outcome sets and adapted for this review (**Supplement Table 3**, available at Annals.org) (22–24). We included studies that reported any outcome related to respiratory infection transmission and excluded studies that only reported outcomes unrelated to respiratory infection transmission.

Search Strategy

An information specialist (J.T.) designed a comprehensive electronic search strategy using a combination of controlled vocabulary and keywords. The search was initially developed for MEDLINE (Ovid) and was peer-reviewed by a second information specialist following the PRESS (Peer Review of Electronic Search Strategies) statement for systematic reviews (25). It was then translated to other databases and run on 12 December 2023 with no date limitation (**Supplement Table 4**, available at Annals.org). We limited the searches to studies published in English and excluded reviews, comments, editorials, interviews, news articles, and letters as publication types. Due to the large number of studies included and resource limitations, we modified our protocol to eliminate the supplemental search for articles cited by included studies.

Eligibility Screening and Data Collection

We deduplicated records before initiating screening. We piloted title, abstract, and full-text screening criteria to ensure consistency across screeners. Screening was performed independently by 2 of 9 trained screeners (A.B., B.F., C.B., J.W., L.C., L.B., L.L., N.B., and S.P.) using Covidence. Discrepancies were resolved by a senior screener (A.B. or L.B.).

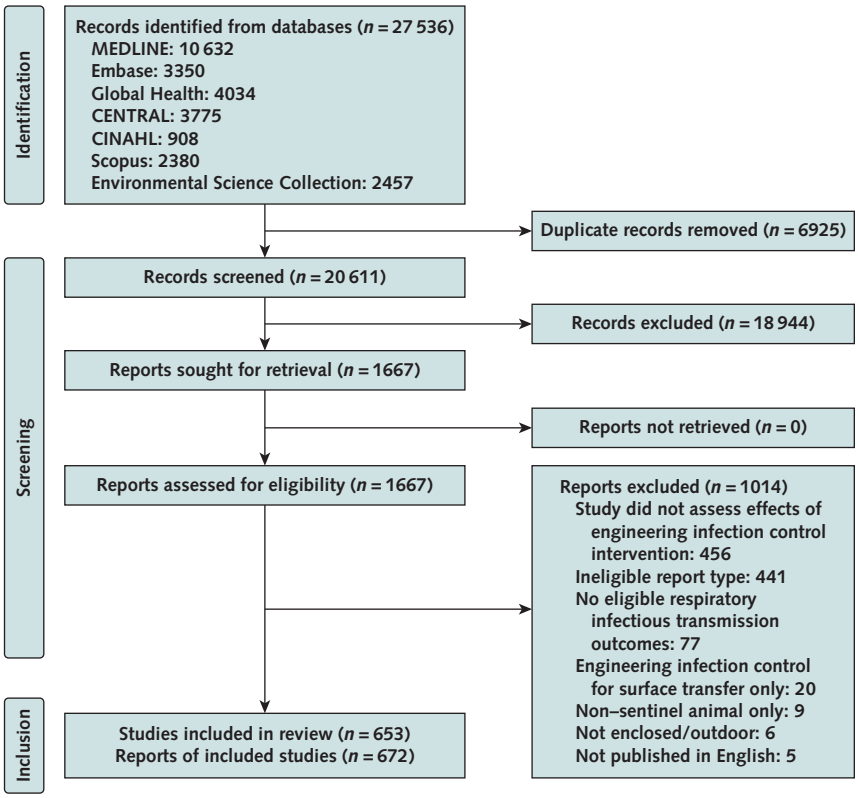
Full-text reports of potentially relevant citations were screened, and reasons for exclusion were recorded according to a hierarchy (**Figure 1**). We performed quality checks beyond those proposed in our protocol. Reviewers who authored studies that were eligible for inclusion in this review did not screen, extract data from, or evaluate their own studies.

Data Extraction

We developed and piloted data extraction and coding forms in the web-based platform Qualtrics. One of 9 reviewers (A.B., B.F., C.B., J.W., L.C., L.B., L.L., N.B., or S.P.) extracted and coded data, which were then verified by a senior reviewer (A.B. or L.B.) (26, 27). Due to the large number of studies, we did not contact study authors for clarification as proposed in our protocol. Extracted data were exported from Qualtrics by one author (L.L.) and checked by a second author (A.B. or L.B.) before analysis. The data extraction form, extracted data, and training materials are available at https://osf.io/5zmhd.

We extracted publication details, study information, population information (for example, National Institutes of Health demographic information, sentinel animal species), intervention details (**Supplement Table 2**), and all relevant outcomes (**Supplement Table 3**). We

Figure 1. Flow diagram of study selection.



CENTRAL = Cochrane Central Register of Controlled Trials; CINAHL = Cumulative Index to Nursing and Allied Health Literature.

categorized studies into 3 main types: 1) human (those evaluating the effect of interventions on infection transmission in humans), 2) sentinel animal (those evaluating the effect of human pathogen transmission in sentinel animals), and 3) environmental (those performed in chamber or real-world settings and examining intervention effects on air or surface microbial loads, particulate matter [PM] counts, and tracer gas concentrations). For human studies, we also examined characteristics that stratify health outcomes alongside context-specific health inequity–related variables (28, 29). For studies evaluating multiple engineering controls, we recorded whether the interventions were assessed individually (for example, local exhaust ventilation with and without high-efficiency particulate air [HEPA] filter) or in a bundle (for example, in-room air cleaner with GUV energy, HEPA filter, and ionizer evaluated as a single intervention).

Evaluation of Included Studies

Through consensus of team members, we developed a system to rate the value of study outcome measures based on their relevance to infection transmission in humans (Supplement Table 5, available at Annals.org). For example, human laboratory-confirmed respiratory infections received the highest outcome value rating of 14, whereas presence or quantity of non-biological compounds, such as tracer gases measured in chamber studies, received the lowest ratings of 1 and 2, respectively. As per scoping review methods, we did not assess risk of bias for primary studies due to the heterogeneity of the included studies (18).

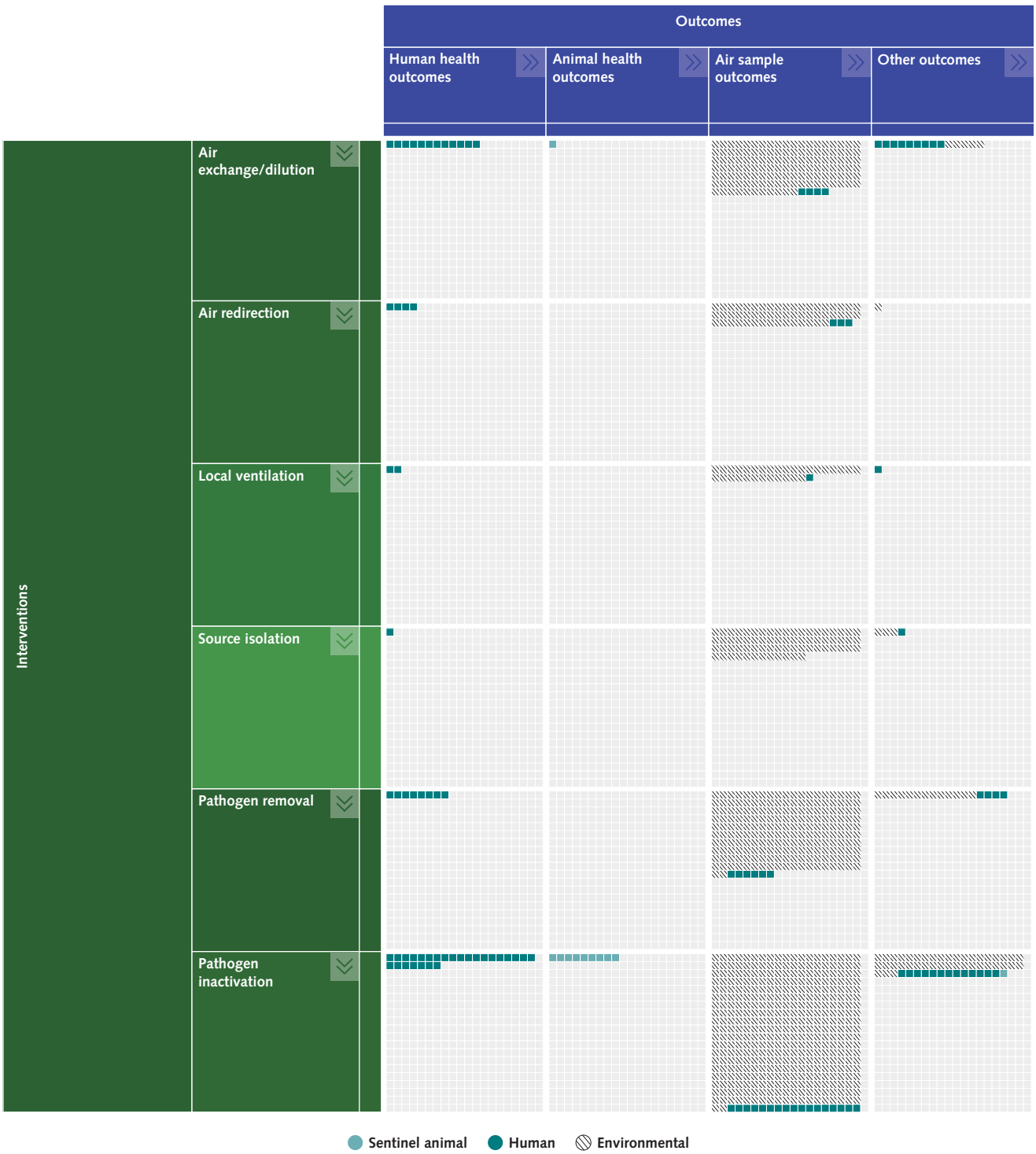
Data Synthesis

The unit of analysis is the individual study rather than the study report (published journal article). If the publication was one of multiple ones for a single study, we merged all study reports. If a publication reported multiple studies, we extracted data and synthesized them separately for each study. We present a descriptive synthesis according to recommendations for scoping reviews (30) and provide numerical summaries, text, and an interactive evidence map.

Role of the Funding Source

Seven of the authors were employed by the funding organization (National Institute for Occupational Safety and Health at the Centers for Disease Control and Prevention [NIOSH/CDC]) at the time this study was conducted. Due to their employment, the final submitted version of the manuscript was reviewed and approved by NIOSH/CDC. This resulted in minor edits to the manuscript but no changes in data or analysis. Otherwise, the funder was not involved in the design, conduct, or publication of this study.

Figure 2. Evidence map of studies of engineering infection controls to reduce indoor transmission of respiratory infections, by intervention and outcome classification ($n = 672$).



The identified studies are visually displayed by intervention and outcome and segmented by study type. In a mosaic map, each box represents 1 study, and the color represents the study type (human, animal, or environmental). Studies that reported on more than 1 intervention or more than 1 outcome are mapped to more than 1 cell.

Table 1. Characteristics of Included Studies of Engineering Infection Controls to Reduce Indoor Transmission of Respiratory Infections ($n = 672$)

Characteristic	Study Type, *n*			Total ($n = 672$)
	Environmental ($n = 606$)	Sentinel Animal ($n = 9$)	Human ($n = 57$)	
Setting*				
Educational facility	43	0	18	61
Health care facility	194	3	25	222
Residential building	20	0	11	31
Transportation conveyance	24	0	1	25
Additional workplaces or facilities	43	0	2	45
Mobile units	2	0	0	2
Chamber (full-size)	108	0	0	108
Chamber (scaled)	180	2	0	182
Sentinel animal living facility	0	7	0	7
Other	11	0	0	11
Not reported	0	0	0	0
Unclear	1	0	0	1
WHO region				
Africa	3	0	0	3
The Americas	230	8	37	275
South-East Asia	28	0	2	30
Europe	155	0	12	167
Eastern Mediterranean	15	0	0	15
Western Pacific	159	1	6	166
Not reported	8	0	0	8
Unclear	8	0	0	8
Funding source*				
Government	315	7	21	343
Industry				
Construction/ engineering/ manufacturing	75	1	8	84
Pharma/biotech	27	0	4	31
Transportation	1	0	0	1
Other	9	0	0	9
Nonprofit or foundation	70	4	6	80
Self-funded or not funded	31	0	5	36
Other	67	2	6	75
Not reported	128	2	18	148
Unclear	3	0	1	4
COIs				
Some authors reported COI	68	2	7	77
All authors reported no COI	275	1	15	291
Missing/unclear COI statement	263	6	35	304

COI = conflict of interest; WHO = World Health Organization.
* Studies could report more than 1 setting or funding source.

RESULTS

Search and Screening

Our database search found 27 536 records. After removing duplicates, we screened 20 611 records and reviewed 1667 full texts. We excluded 1014 study reports; reasons are shown in **Figure 1**. We included 672 studies (653 study reports); 22 reports included unique results from 2 studies ($n = 44$ reports), and 3 studies had multiple reports ($n = 6$ reports). Included studies can be downloaded from the interactive evidence map at https://osf.io/5zmhd.

Evidence Map

Figure 2 shows an evidence map visualizing clusters of studies by interventions tested, outcomes measured, and study type. An interactive evidence map is available at https://osf.io/5zmhd.

Study Characteristics

Table 1 shows the characteristics of the 672 included studies. The majority (90% [606 of 672]) were classified as environmental studies, 8% (57 of 672) were classified as human studies, and 1% (9 of 672) were classified as sentinel animal studies. More than half were published in 2020 or later, with a progressive increase in all study types between 2000 and 2020 (**Supplement Figure 2**, available at Annals.org). Real or simulated health care facilities, such as hospital rooms, were the most common study setting (33% [222 of 672]).

In 2% (16 of 672) of studies, the study or author location was unclear or not reported. Studies came from all 6 World Health Organization regions (**Table 1**), including the Americas (41% [275 of 672]), Europe (25% [167 of 672]), and the Western Pacific (25% [166 of 672]). Only 3 studies were from Africa.

Funding statements were unclear or not reported in 23% (152 of 672) of included studies (**Table 1**). Of the studies with funding statements, 30% (154 of 520) had multiple funding types. The majority (66% [343 of 520]) reported government funding. Conflict of interest (COI) statements were missing or unclear in 45% (304 of 672) of studies, which included 1342 authors (median, 4 authors [IQR, 2 to 6]; range, 1 to 15 authors). In 291 studies with a total of 1854 authors (median, 6 authors [IQR, 3 to 7]; range, 1 to 19 authors), none of the authors had a COI. For the other 77 studies, 40% (215 of 542 study authors) had 1 or more reported COIs (median, 33% [IQR, 20% to 57%]; range, 6% to 100%).

Fifty-seven studies investigated the effects of engineering infection controls on humans (**Supplement Table 6**, available at Annals.org), with 248 716 participants included (median, 270 participants [IQR, 90 to 1100]; range, 26 to 205 347 participants), although the number of participants was reported for only two thirds (38 of 57) of the studies. There were 6 randomized controlled trials conducted between 1951 and 2022 and 51 observational studies published between 1929 and 2023. Sex was reported in 44% of studies (25 of 57); 5 studies included males only, and 20 included males and females. Racial demographics were reported in 23% of studies (13 of 57), and ethnicity was reported in 9% (5 of 57). The majority of studies (58% [33 of 57]) included children only (aged <18 years), 17 included

adults, and 7 did not report the age of participants. No studies reported pregnant, in utero, or postpartum age groups or populations. Nineteen percent (11 of 57) included characteristics that could allow subgroup analysis or stratification for equity analysis. Several earlier studies (from before the 1980s) with unclear consent processes included populations such as minors, orphans, institutionalized persons, and military personnel. Human studies examined transmission of myriad bacterial and viral infections, with 5 studies focusing on SARS-CoV-2 and 5 focusing on influenza.

Nine studies used sentinel animals to study mediation of human infection transmission. These included guinea pigs ($n = 3$), mice ($n = 2$), rabbits ($n = 2$), hamsters ($n = 1$), and chicken embryos ($n = 1$). The majority of these studies were published between 1944 and 1965 ($n = 6$). The number of animals studied was reported in 8 of the 9 studies (median, 70 animals [IQR, 27 to 253]; range, 6 to 450 animals). Six studied mycobacteria, with 4 evaluating *Mycobacterium tuberculosis*.

Most studies were environmental (90% [606 of 672]) and conducted in chambers ($n = 288$), of which 180 were scaled chambers and 108 were full-sized chambers. Other commonly studied settings included health care facilities ($n = 194$), educational facilities ($n = 43$), other workplaces ($n = 43$), transportation conveyances ($n = 24$), and residential buildings ($n = 20$) (Table 1). Environmental studies often explored intervention effects on specific bacteria ($n = 194$), viruses ($n = 124$), and general airborne bacterial load ($n = 137$). The most commonly studied outcome was the quantity of viable nonpathogenic microorganisms ($n = 316$), followed by the quantity of nonbiological particulates ($n = 191$), viable pathogenic organisms ($n = 139$), and nonbiological compounds ($n = 65$) (Table 2).

Interventions Studied

Table 2 shows the intervention classifications by study type. There were a total of 1073 interventions in the 672 included studies. Most studies (61% [408 of 672]) examined a single engineering control intervention. Multiple interventions were examined in 264 studies, of which 131 assessed multiple interventions individually (range, 2 to 5 interventions per study), 88 studied only intervention bundles (range, 1 to 3 bundles), and 45 examined both bundled and nonbundled interventions. Most commonly, bundles included HEPA filters combined with another intervention, such as GUV energy ($n = 14$ studies), barrier enclosure ($n = 8$), or local exhaust ventilation ($n = 5$). The number of studies examining pathogen inactivation interventions has accelerated since 2000, and studies of all other interventions have increased since 2020.

At the broadest intervention classifications, 78% of studies (526 of 672) included 1 or more interventions in the pathogen capture or inactivation category, 38% (254 of 672) included 1 or more interventions in the air or pathogen movement category, and 16% (108 of

Table 2. Intervention Classification, by Study Type ($n = 672$)*

Intervention Classification	Study Type, *n*			Total
	Environmental	Sentinel Animal	Human	
Air exchange or dilution†	125	1	17	143
Mechanical ventilation	87	0	15	102
Natural ventilation with an opening manipulation	47	0	6	53
Other natural ventilation	5	0	1	6
Hybrid ventilation				
Fan for air mixing	16	1	1	18
Exhaust fan	9	0	2	11
Other	8	0	1	9
Air redirection†	53	0	4	57
Displacement ventilation	11	0	0	11
Laminar flow ventilation	8	0	3	11
Downward ventilation	10	0	0	10
Negative-pressure ventilation	19	0	1	20
Positive-pressure ventilation	7	0	2	9
Stratum ventilation	7	0	0	7
Local ventilation†	31	0	2	33
Local exhaust ventilation				
Extra-oral dental suction	14	0	1	15
Suction built into an aerosol-generating device	2	0	0	2
Other	8	0	0	8
Local supply ventilation	7	0	0	7
Protected occupied zone ventilation	3	0	1	4
Source isolation†	69	0	1	70
Barrier enclosure, with or without suction	44	0	0	44
Anteroom	6	0	1	7
Plexiglass/shields	16	0	0	16
Waste management	3	0	0	3
Pathogen removal†	192	0	8	200
Mechanical filter				
Coarse	22	0	0	22
Medium	3	0	0	3
Fine	23	0	0	23
Efficient particulate air	1	0	0	1
High-efficiency particulate air	131	0	6	137
Ultra-low particulate air	6	0	0	6
Filter rating unclear/not specified	19	0	2	21
Other	18	0	1	19
Breathing circuit filter	2	0	0	2
Pathogen inactivation†	363	9	33	405
Germicidal ultraviolet energy	166	6	20	192
Photocatalytic oxidation	43	0	1	44
Nanocomposite filters	43	0	0	43
Ionization	42	2	3	47
Plasma-based technologies	35	0	0	35
Other electronic air cleaner	12	0	0	12
Ozone generator	12	0	1	13
Humidity control	16	0	2	18
Thermal energy	5	0	0	5
Ambient temperature control	6	0	0	6
Nebulized/vaporized bactericides	31	2	7	40
Other	11	0	0	11

* Studies could test more than 1 intervention or bundles of interventions.
† Studies could report more than 1 intervention strategy under the highest level of classification.

Table 3. Outcome Value Rating, by Study Type ($n = 672$)*

Outcome Value Rating†	Outcome Description	Study Type, *n*			Total
		Environmental	Sentinel Animal	Human	
14	Human laboratory-confirmed respiratory infection	0	0	17	17
13	Human non–laboratory-confirmed respiratory illness	0	0	35	35
12	Sentinel animal laboratory-confirmed respiratory infection	0	9	0	9
11	Sentinel animal non–laboratory-confirmed respiratory illness	0	0	0	0
10	Quantity of viable pathogenic microorganism	139	2	8	149
9	Presence of viable pathogenic microorganism	5	0	4	9
8	Quantity of viable nonpathogenic microorganism	316	1	15	332
7	Presence of viable nonpathogenic microorganism	5	0	1	6
6	Quantity of microbial constituent or product	23	0	0	23
5	Presence of microbial constituent or product	5	0	0	5
4	Quantity of nonbiological particulates	191	1	5	197
3	Presence of nonbiological particulates	24	0	0	24
2	Quantity of nonbiological compounds	65	0	4	69
1	Presence of nonbiological compounds	5	0	0	5

* Studies could report multiple outcomes with different outcome ratings.
† Outcomes were rated for their relevance to infection transmission in humans, with 14 indicating highest relevance and 1 indicating lowest relevance.

672) included both. At the intervention strategy level, most of the studies had 1 or more interventions categorized as pathogen inactivation (60% [405 of 672]), followed by pathogen removal (30% [200 of 672]), air exchange or dilution (21% [143 of 672]), source isolation (10% [70 of 672]), air redirection (8% [57 of 672]), and local ventilation (5% [33 of 672]) (Table 2).

In the air movement category, the most commonly studied interventions included mechanical ventilation ($n = 102$), natural ventilation ($n = 59$), barrier enclosures ($n = 44$), hybrid ventilation ($n = 38$), and negative-pressure ventilation ($n = 20$) (Table 2). In the pathogen capture and inactivation categories, the most commonly studied interventions included GUV energy ($n = 192$), HEPA filters ($n = 137$), ionization technologies ($n = 47$), photocatalytic oxidation ($n = 44$), nanocomposite filters (mechanical filters incorporating inactivating agents; $n = 43$), nebulized or vaporized bactericides ($n = 40$), and plasma-based technologies ($n = 35$). Among the GUV studies, there were 17 with LED-based UV light and 2 with pulsed-xenon UV light. Of the studies that reported the UV wavelength ($n = 123$), the majority evaluated 254 nm ($n = 92$), and some tested far-UV light at 222 nm ($n = 15$). The intervention technologies that did not fit our prespecified scheme included electric fields ($n = 1$), microwaves ($n = 2$), far-infrared light ($n = 1$), organic-based antimicrobial-coated filters ($n = 4$), and antimicrobial surface coating of internal heating, ventilation, and air conditioning (HVAC) components with copper ($n = 1$) or nanosilver paint ($n = 2$).

Supplement Table 7 (available at Annals.org) details whether the pathogen capture or inactivation technologies were studied in-duct (HVAC), as part of an in-room air cleaner, or in a scaled chamber and shows that all interventions were most frequently studied as part of an in-room air cleaner. Studies were often conducted in mechanically ventilated spaces ($n = 216$), but many used unventilated spaces ($n = 103$) or did not report background engineering controls ($n = 82$). Of the 256 background engineering settings documented in studies involving in-room air cleaners, about half used ventilated spaces, including mechanical ($n = 108$), natural ($n = 20$), or hybrid ($n = 11$) ventilation, while many were in unventilated spaces ($n = 63$) or did not report background controls ($n = 38$).

Relevance of Outcomes for Human Infection Transmission

Table 3 shows the outcome value ratings by study type, with a rating of 14 indicating the highest relevance for transmission of human infection and a rating of 1 indicating the lowest relevance. Of a total of 957 reported outcomes in 672 studies, 49% of studies (332 of 672) measured the quantity of viable nonpathogenic organisms in cultures collected from air samples (outcome value rating of 8). This was most often measured as general bacterial, viral, or fungal load and thus could not be linked to specific organisms. The quantity of nonbiological particulates (outcome value rating of 4) was the next most commonly measured outcome (29% [197 of 672]); this included measurement of synthetic particles generated to specific size ranges and PM, such as dust, smoke, or spores. The quantity of viable pathogenic organisms (outcome value rating of 10) was the third most commonly studied outcome (22% [149 of 672]).

Seventy-seven studies reported relevant outcomes outside of direct or indirect infection transmission. Twenty-four human studies reported such outcomes, with 16 reporting school or work absenteeism or time to or rate of return to school or work (documented by the school or workplace or self-reported), 5 assessing acceptability of the intervention, and 2 reporting adverse effects. None measured quality of life or functioning; none measured sustainability, such as carbon footprint or greenhouse gas emissions; and none included economic analysis.

Among the pathogen inactivation technologies, nanocomposite filters, plasma-based technologies,

other electronic air cleaners, thermal energy, ambient temperature control, and "other" inactivation technologies were tested only in environmental studies (Table 2). Of the 112 studies examining these interventions, only 14 examined harmful byproducts, such as ozone, formaldehyde, carbon monoxide, hydroxyls, or hydrogen peroxide. Thirteen environmental studies measured acceptability of the intervention, such as noise, ambient temperature and humidity comfort, or environmental odor control.

DISCUSSION

We examined the published evidence evaluating engineering infection control interventions to prevent the spread of respiratory infections transmitted among people through indoor air. We found that most of these evaluations are environmental studies that measure surrogate outcomes rather than direct human infectious outcomes. Studies measuring outcomes in humans were largely observational and were often conducted in health care settings.

The most frequently studied interventions involved pathogen inactivation, pathogen removal via HEPA filters, or air exchange or dilution, although source isolation, local ventilation, and airflow redirection were also evaluated. GUV energy was the most often studied pathogen inactivation intervention, and newer methods such as photocatalytic oxidation, nanocomposite filters, ionization, and plasma-based technologies were also evaluated. These inactivation technologies were primarily studied in chambers or as a component of in-room air cleaners and, less commonly, in HVAC ducts.

Most studies measured environmental indicators as surrogate outcomes in air samples, not human health data, reflecting the predominance of environmental study designs in the literature. Using an outcome rating developed for this review to assess relevance to the transmission of infections among persons, we found that environmental studies often focused on viable nonpathogenic organisms, with viable pathogenic microorganisms less frequently used. Many studies, particularly those evaluating interventions affecting pathogen movement through the air, used nonbiological particulates (synthetic particles, PM counts) as surrogates.

Overall, few studies directly examined the effects of engineering control interventions on human-to-human indoor transmission of respiratory pathogens. There are many reasons for this lack of research, including ethical standards that restrict experimental exposure of humans to known pathogens and the relatively high cost of conducting human health studies compared with studies involving laboratory surrogates (31) or environmental surrogates (32). Indeed, half of the human studies identified in this review were conducted before the 1980s, before the enactment of today's ethical requirements for human participant research (33). Additional challenges to conducting human studies include enrolling sufficiently large samples to allow for detection of differences between intervention and control groups and to enable control, by design or analysis, for factors that could confound clinical effects of the engineering infection control intervention being studied. Advanced causal inference designs and analytical approaches to address potential biases in observational studies could address these methodological issues (34, 35). Although challenging, human studies are important to understand effectiveness in reducing human infections. In addition, research to validate surrogate outcomes measured in chamber studies against human health effects is an ongoing need.

Few included studies measured potential harms from engineering controls, complicating harm–benefit assessment. Measured harms were usually intervention-specific, such as ozone formation from GUV light, ionizers, plasma generation, or photocatalytic oxidation. The paucity of studies measuring harms creates concerning gaps in knowledge since there is evidence that these technologies can produce byproducts that can harm human health (36, 37). No studies reported on potential environmental harms, sustainability outcomes, or cost-effectiveness analyses, although some noted intervention design costs. Potential inequities in harms or efficacy were not addressed. Human studies generally reported age and sex but rarely provided data for equity analysis. This review focused on interventions used to reduce transmission of infection or exposures used as surrogates of infection, so studies solely addressing cost, harms, or equity without evaluating intervention effectiveness were excluded, limiting inference about the breadth of such literature.

In-room air cleaners involving pathogen inactivation technologies are already marketed to consumers, yet we found that evaluations of these technologies are rarely done in humans and often do not assess harmful byproducts. These findings highlight the importance of more rigorous assessment through primary research evaluating their effectiveness and harms before these products are available to the public.

We attempted to classify the studied environmental samples as pathogenic versus nonpathogenic microbes since preventing the spread of pathogenic microbes is most relevant to human health. However, several challenges made this classification difficult. First, most studies measured total environmental microbial load rather than specific microbes. We classified these as nonpathogenic samples. Second, some quantitatively measured specific microbes were difficult to classify as pathogenic or nonpathogenic. Some are clearly pathogenic in most clinical scenarios (such as influenza, SARS-CoV-2, respiratory syncytial virus, and *M tuberculosis*), whereas others are clearly nonpathogenic (such as bacteriophages, *Escherichia coli* K12, and *M smegmatis*). However, others have context-dependent pathogenicity, such as *Aspergillus fumigatus*, which can cause serious infections on bone marrow transplant wards while being less harmful in other settings or clinical scenarios (for example, in a building with healthy adults). Similarly,

some microbes, such as *Staphylococcus aureus*, can be pathogenic but may not necessarily be primary respiratory pathogens. Therefore, more nuance in describing the pathogenicity of organisms in a particular study context would be beneficial. Reporting could indicate whether microbes are pathogenic but nonrespiratory or pathogenic only under the specific conditions examined in a study.

We identified large heterogeneity of outcome measures among studies included in this review. Researchers evaluating engineering infection controls could develop core outcome sets, similar in concept to those that are widely used in clinical and epidemiologic research (38). Core outcome sets provide a minimum group of outcomes that should be measured in all studies on a particular topic, with the option to evaluate additional outcomes. When core outcomes are reported, results of studies can be compared, contrasted, and combined for evidence synthesis.

The outcome value rating developed for this scoping review provides an overview of the relevance of measured outcomes for affecting transmission through the air of organisms that infect humans. In addition, we suggest ways to further enhance outcome reporting and the informativeness of the outcome rating. First, certain outcomes may be irrelevant for specific pathogen-inactivation technologies. For instance, concentrations of tracer gases, such as carbon dioxide, are unlikely to be a relevant outcome for GUV technologies. The outcome value rating could be adjusted to indicate that some outcomes are only pertinent to interventions that move or filter air. Second, although pathogen colonization was a commonly measured outcome, there was variation in how the air or surface samples were collected. For instance, air microbial sampling techniques ranged from active methods (for example, 6-stage Andersen sampler) to passive methods (for example, settle plates), and surface samples included colonization on personal protective equipment or human nares as outcomes. Because sampling techniques can influence measured outcomes and affect the true relevance of surrogate outcomes to human exposure, these techniques could be factored into the outcome value rating scheme. Third, guidance is needed to correctly classify certain viral assays, such as focus-forming assays, fluorescent focus units, and hemagglutination assays. When applying an outcome rating scheme, it may be beneficial to list all known assays and specify whether they assess viable microbes or microbial constituents or products. Fourth, under the current outcome rating scheme, PM and tracer gases were included as eligible outcomes. Some studies do not report these measurements directly but use them to calculate related outcomes, such as "age of air," "infection probability," or air change rate (for example, via tracer gas decay). Future application of an outcome rating could clarify how studies that measure eligible outcomes (such as PM or tracer gas) but report only calculated outcomes (such as age of air or change in air changes per hour) should be rated. These suggested modifications to the outcome rating approach used in this review could help future systematic reviews assess the relevance of outcome measures for transmission of infection by air to humans and shape the reporting guidelines for primary studies. This outcome assessment could be a useful addition to the standard internal validity or risk of bias assessment done for studies included in systematic reviews.

Recent systematic reviews have focused on specific settings, pathogens, or interventions. One systematic review evaluated the relationship between ventilation parameters, such as ventilation rate and transmission of coronaviruses, but did not examine other pathogens that spread through air (6). Another systematic review of studies conducted in hospital environments examined the relationship between HVAC systems, with and without specific additional features such as HEPA filters and laminar flow, and ambient air microbial colony counts (3). HVAC-integrated mechanical filters were assessed in a review that included 23 animal, modeling, and aerosolized virus studies and correlated filtration rating with viral transmission (7). A related systematic review examined the role of GUV energy in human, animal, aerosolized virus, and bacteriophage studies (5).

The findings of this scoping review identify clusters of studies that allow formulation of specific research questions that warrant further analysis through systematic review. Previous reviews have not examined HVAC-integrated germicidal technologies, such as bipolar or cold plasma ionization, nanocomposite filters, or photocatalytic oxidation (39–42). The findings of this scoping review suggest that there are sufficient studies to conduct reviews of these latter types of germicidal technologies. We also found studies exploring innovative technologies, including nanocomposite photocatalytic filters that aim to work without UV-C light and laser-induced graphene technologies that use low-voltage electrical impulses to kill microbes (43–45). To plan for evidence synthesis at the forefront of this science, there is a need to develop a comprehensive conceptual intervention framework that can accommodate these new technologies while remaining flexible for completely new advancements.

The large number of chamber studies we identified that measure similar surrogate outcomes suggests topics for systematic reviews. For example, systematic reviews of chamber studies of similar interventions could explore how chamber characteristics (such as size or air mixing) and pathogen source (for example, type of pathogen or surrogate, method for dispersing the pathogen in the chamber) influence the measured efficacy of the interventions. Network analysis across intervention types examined in chamber studies could also provide information on the relative effectiveness of different interventions studied under similar conditions. In addition, conducting systematic reviews of chamber studies would require an assessment of the

internal validity of each study included in a review, thus allowing the conclusions of reviews to be based on the most rigorous studies. The large heterogeneity in the human and animal studies we identified suggests limited numbers of these types of studies for systematic review.

This review has several limitations. We conducted a comprehensive search identifying almost 700 studies for inclusion. However, we did not conduct a search of the gray literature and limited the search to English-language publications only, so we may have failed to identify relevant studies. We included sentinel animal studies of human infections and studies of animal pathogens conducted in chambers but excluded studies of infections in animals only. We may have inadvertently excluded studies of engineering infection controls using animal models of pathogens that can infect humans via transmission through the air. We included studies that measured effectiveness and harms of interventions but did not search for studies that measured only harms. Therefore, we could have missed some studies that measured harms only. We excluded a recent study that used cameras to evaluate light refraction to infer air movement because this was not considered an eligible outcome (46). As researchers develop innovative methods to evaluate air movement, filtration, or other parameters of engineering infection control function, it could be helpful to establish overarching principles for determining the eligibility of new surrogate outcome measures for engineering infection control.

In conclusion, this review identified substantial variability in studies evaluating the effects of engineering infection controls on transmission of human respiratory infections. Gaps in evidence include studies measuring harms or efficacy outcomes that are highly relevant for human-to-human transmission of infection. Refinements in intervention and outcome classification could strengthen reporting of these evaluations. Future systematic reviews of newer pathogen inactivation technologies and of studies conducted in chambers could provide data on factors that modify efficacy of interventions.

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Note: Drs. Radonovich, Bahnfleth, Mead, and Olsiewski have authored studies that could be eligible for inclusion in this review. These authors were not involved in screening, data extraction, or evaluation of studies on which they were authors.

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