ENVE 576
Indoor Air Pollution
Summer 2020

Lecture 12 – Finish epidemiology and adverse health effects & Indoor microbiology

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Schedule updates from last week

6	July 6	July 7	Lecture 10: SVOCs & Health effects and epidemiology	32–35, 37–40	HW #3 due
		July 10 (Fri)	Lecture 11: IAQ measurement techniques + *IAQ sensor activity*	36	Sensor activity assignment & Blog #2 due
7	July 13	July 14	Lecture 12: Finish health effects and epidemiology & Indoor microbiology	41–44	
		July 17 (Fri)	Lecture 13: Airborne infectious disease transmission	45–47	HW #4 due
8	July 20	July 21	Lecture 14: IAQ in developing countries & IAQ Applications • Standards/ratings & computer modeling	48–50 51–54	
		July 23	Reserve for unfinished lecture materials		Blog #3 due
9+	Aug 10	Aug 10	Final project presentations and reports due		Final presentations Final report

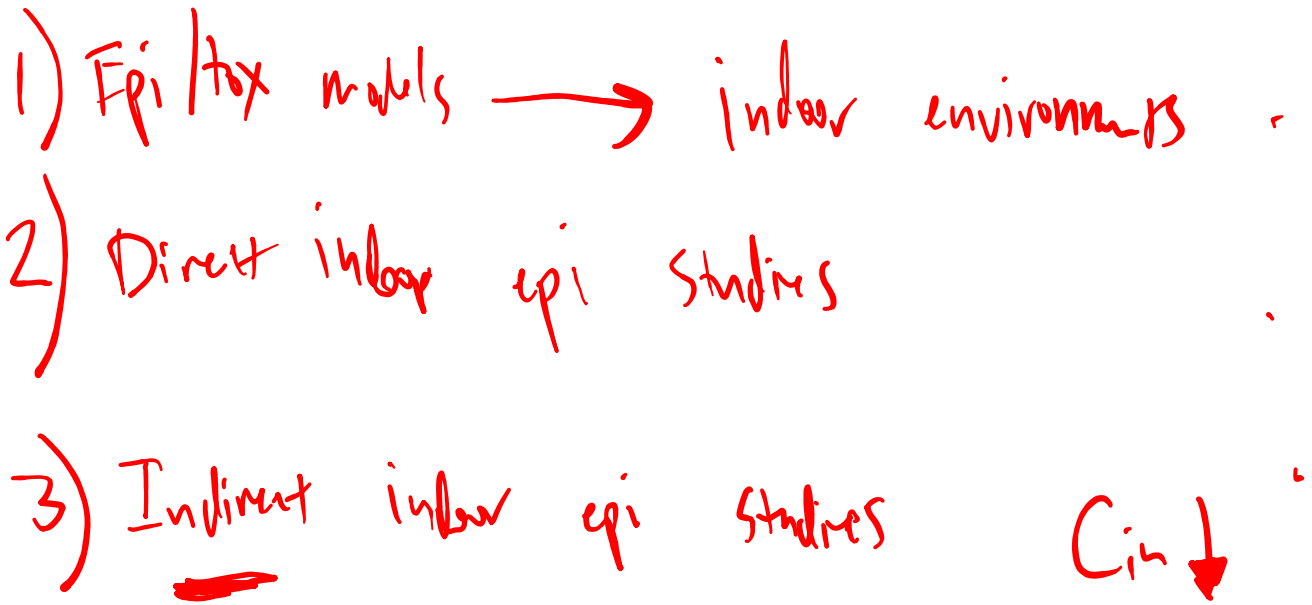
Final project presentations and reports now due **Monday, August 10**

- Submit final report by class time (11:30 am central time)
- For those who can, present in class (11:30 am central time)
- For those who can't, upload your recording

Final blog post due July 23: the topic is entirely up to you

Follow up from last week

- Health effects and epidemiology
  - Biological plausibility from cell/animal models
  - Associations in human epidemiology studies
  - Focused on outdoor air
    - And began to link outdoor air to indoor exposures
    - Will finish this today
- Indoor air quality measurement techniques
  - Low cost sensor exercise
- The rest of this week:
  - Focus on microbiology (broadly), as well as infectious disease transmission



LINKING INDOOR AIR AND EPIDEMIOLOGY

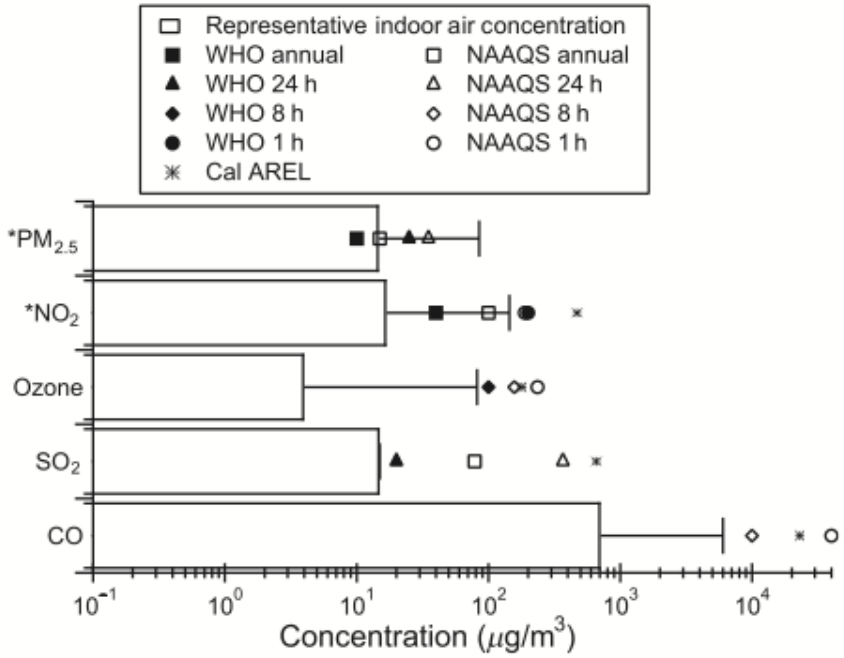
Combining epidemiology and toxicology studies to model health outcomes of indoor exposures

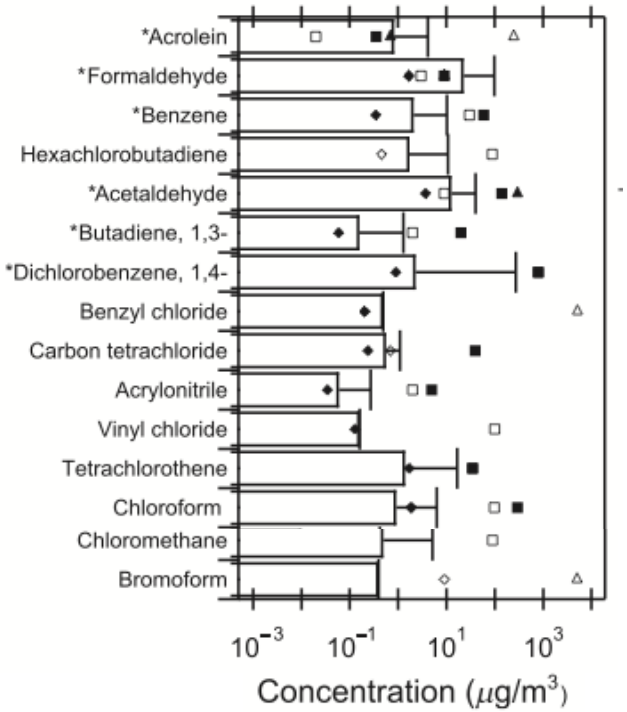
Hazard assessment of chemical air contaminants measured in residences

Logue et al., *Indoor Air* **2010**

Table 1 Publications with chronic exposure-relevant concentrations

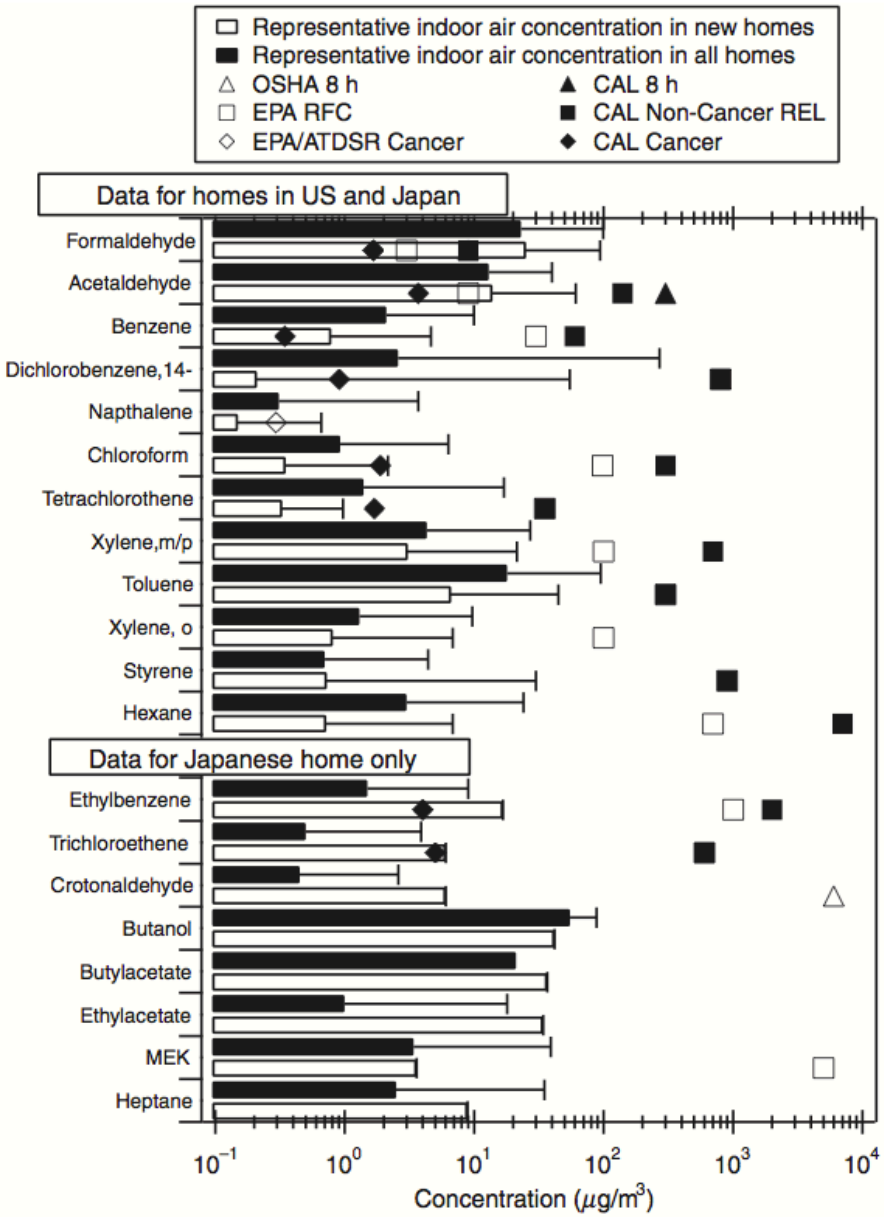
	Study	Sample Period	Location: city, country or US State	US homes	New homes	Criteria pollutants	VOCs	Aldehyde	SVOCs	Metals	Number of samples
1	Topp et al. (2004)	2 weeks	Hamburg/Erfurt, Germany			N	X				2524
2	Park and Ikeda (2006)	24 h	Japan		X		X	X			2151
3	Geyh et al. (2000)	6 months	Upland, CA, USA	X		O					1980
4	Rehwagen et al. (2003)	4 weeks	Leipzig, Germany				X		X		1499
5	Garcia-Algar et al. (2003)	7–15 days	UK, Spain			N					1438
6	Williams et al. (2009)	5 days	Detroit, MI, USA	X		P					973
7	Lee et al. (1998)	48 h	Boston, MA, USA	X		N					942
8	Raw et al. (2004)	2 weeks	England, UK			N, C					812
9	Levy (1998)	48 h	Various Cities, North America,	X		N					617





Hazard assessment of chemical air contaminants measured in residences

Logue et al., *Indoor Air* **2010**



"Fifteen pollutants appear to exceed chronic health standards in a large fraction of homes. Nine other pollutants are identified as potential chronic health hazards in a substantial minority of homes, and an additional nine are identified as potential hazards in a very small percentage of homes. Nine pollutants are identified as priority hazards based on the robustness of measured concentration data and the fraction of residences that appear to be impacted: acetaldehyde; acrolein; benzene; 1,3-butadiene; 1,4-dichlorobenzene; formaldehyde; naphthalene; nitrogen dioxide; and $PM_{2.5}$. Activity-based emissions are shown to pose potential acute health hazards for $PM_{2.5}$, formaldehyde, CO, chloroform, and NO_2."

A Method to Estimate the Chronic Health Impact of Air Pollutants in U.S. Residences

Logue et al., *Environ Health Persp* **2012**

$$DALY_{disease} = YLL_{disease} + YLD_{disease}$$

$$DALYs = (\partial DALYs/\partial disease\ incidence) \times disease\ incidence.$$

Intake-incidence-DALY approach

$$\Delta Incidence = -\{y_0 \times [\exp(-\beta \Delta C_{exposure}) - 1]\} \times population,$$

$$\Delta C_{exposure} = 0.7 C_{indoors}$$

Intake-DALY approach

$$DALYs = (\partial DALY/\partial disease\ incidence) \times (\partial disease\ incidence/\partial intake) \times intake,$$

$$DALYs_i = (\partial DALY/\partial intake) \times intake,$$

$$DALYs_i = C_i \times V \times [(\partial DALY_{cancer}/\partial intake)_i \times ADAF + (\partial DALY_{noncancer}/\partial intake)_i],$$

The DALY metric allows quantification and comparison of the health costs from varied disease end points that can result from various pollutants. As a measure of equivalent years of life lost (YLL) due to illness or disease, DALY loss quantifies overall disease costs (impacts) due to both mortality and morbidity. DALY losses include YLL due to premature mortality and equivalent YLL due to reduced health or disability (YLD). For each disease, the DALYs lost per incidence are calculated as follows:

$$DALY_{disease} = YLL_{disease} + YLD_{disease}. \quad [1]$$

The equivalent life-years lost to reduced health are weighted from 0 to 1 based on the severity of the disease. For example, a 5-year illness that reduces quality of life to 4/5 that of a healthy year is valued at 1 DALY lost.

https://en.wikipedia.org/wiki/Disability-adjusted_life_year

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$$DALYs_i = C_i \times V \times [(\partial DALY_{cancer}/\partial intake)_i \times ADAF + (\partial DALY_{noncancer}/\partial intake)_i],$$

Table 1. Pollutants included in analysis and assumed population-average concentrations (μg/m³).

Pollutant	Concentration	Pollutant	Concentration
1,1,2,2-Tetrachloroethane	0.42	Cyclohexane	5.2
1,1,2-Trichloroethane	0.46	Di(2-ethylhexyl) adipate	1.6×10^{-2}
1,1-Dichloroethene	1.2	Dibenzo[*a*,*c*+*a*,*h*]anthracene	1.4×10^{-5}
1,2-Dibromoethane	0.14	Dibromochloromethane	0.44
1,2-Dichloroethane	0.34	*d*-Limonine	23
1,3-Butadiene	0.46	Ethanol	860
1,4-Dichlorobenzene	50	Ethylbenzene	3.9
2-Butoxyethanol	2.6	Formaldehyde	69
2-Ethylhexanol	3.7	Hexachlorobutadiene	1.7
2-Ethoxyethanol	0.43	Hexane	7.3
2-Methoxyethanol	0.12	Isopropylbenzene	0.4
Acetaldehyde	22	Manganese	3.3×10^{-3}
Acrolein	2.3	Methyl ethyl ketone	7.4
Acrylonitrile	0.27	Mercury	1.6×10^{-4}
Ammonia	28	Methyl methacrylate	0.27
Arsenic	9.8×10^{-4}	Methylene chloride	8.2
Atrazine	5.9×10^{-4}	Methyl isobutyl ketone	1.2
Benzaldehyde	2.5	Methyl *tert*-butyl ether	12
Benzene	2.5	Naphthalene	1.2
Benzo[*a*]pyrene	9.1×10^{-5}	NO_2	13.1
Benzyl chloride	0.5	*o*-Phenylphenol	0.13
Beryllium	1.6×10^{-6}	Ozone	17.2
Bis(2-ethylhexyl) phthalate	0.14	Pentachlorophenol	2.9×10^{-3}
Bromodichloromethane	0.49	$PM_{2.5}$	15.9
Bromoform	0.39	Styrene	5.9
Cadmium	2.6×10^{-3}	SO_2	2.9
Carbon disulfide	0.34	Tetrachloroethene	1.7
CO	810	Tetrahydrofuran	15
Carbon tetrachloride	0.68	Toluene	2.3
Chlorobenzene	0.68	Trichloroethene	0.16
Chloroethane	0.26	Vinyl chloride	1.7
Chloroform	1.5	Xylene, *o*	8.2
Chloromethane	1.8	Xylene, *m*/*p*	9.7
Chromium	2.2×10^{-3}	Xylenes	7.4
Crotonaldehyde	4.7		

A Method to Estimate the Chronic Health Impact of Air Pollutants in U.S. Residences

Logue et al., *Environ Health Persp* **2012**

Effect estimates for the Intake-incidence-DALY approach:

Table 2. Criteria pollutant C-R function outcomes and DALYs lost per incidence.

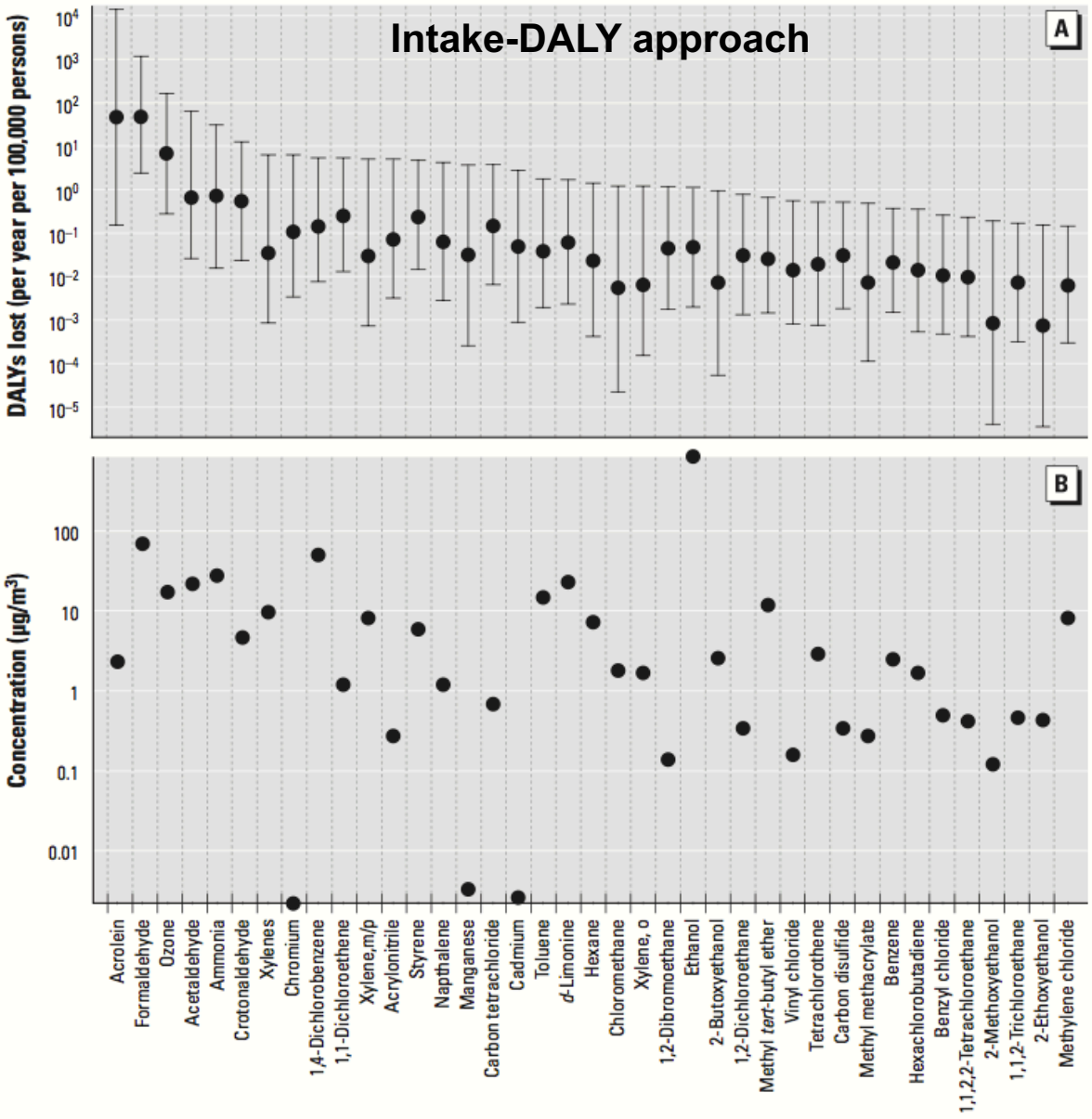
Pollutant	Outcome	β-Coefficient (95% CI)	y_0	DALYs lost per incidence (95% CI)
$PM_{2.5}$	Total mortality (Pope et al. 2002)	0.058 (0.002, 0.010)	7.4×10^{-3}	1.4 (0.14, 14) (Pope 2007; Pope et al. 2002, 2009)
	Chronic bronchitis (Abbey et al. 1995)	0.091 (0.078, 0.105)	0.4×10^{-3}	1.2 (0.12, 12) (Lvovsky et al. 2000; Melse et al. 2010)
	Nonfatal stroke (Brook et al. 2010)	0.025 (0.002, 0.048)	0.2×10^{-3}	0 complications: 9.5 (9.25, 9.75) 1 complication: 11.7 (11.1, 12.4) > 1 complication: 13.1 (12.2, 14.0) (Hong et al. 2010)
CO	Hospital admissions (Burnett et al. 1999)			4×10^{-4} (Lvovsky et al. 2000)
	Asthma	0.033 (0.016, 0.050)	1.8×10^{-3}	
	Lung disease	0.025 (0.000, 0.057)	2.1×10^{-3}	
	Dysrhythmias	0.058 (0.012, 0.102)	2.4×10^{-3}	
	Heart failure	0.034 (0.002, 0.066)	3.4×10^{-3}	
NO_2	Hospital admissions (Burnett et al. 1999)			4×10^{-4} (Lvovsky et al. 2000)
	Respiratory issues	0.004 (0.000, 0.008)	9.5×10^{-3}	
	Congestive heart failure	0.003 (0.001, 0.004)	3.4×10^{-3}	
	Ischemic heart disease	0.003 (0.002, 0.004)	8.0×10^{-3}	
	Respiratory illness, indicated by symptoms (Hasselblad et al. 1992)	0.028 (0.002, 0.053)	N/A	4×10^{-4} (Lvovsky et al. 2000)
Ozone	Mortality (Jerrett et al. 2010; Samet et al. 1997)	0.001 (0.000, 0.002)	7.7×10^{-3}	1.0 (0.1, 10) (Levy et al. 2001; Lvovsky et al. 2000)
	Hospital admissions (Burnett et al. 1999)			4×10^{-4} (Lvovsky et al. 2000)
	Asthma	0.003 (0.001, 0.004)	1.8×10^{-3}	
	Lung disease	0.003 (0.001, 0.005)	2.1×10^{-3}	
	Respiratory infection	0.002 (0.001, 0.003)	5.8×10^{-3}	
	Dysrhythmias	0.002 (0.000, 0.004)	2.4×10^{-3}	
SO_2	Hospital admissions (Burnett et al. 1999)	0.002 (0.000, 0.003)	8.0×10^{-3}	4×10^{-4} (Lvovsky et al. 2000)

N/A, not applicable. y_0 is the baseline prevalence of illness per year, and β is the coefficient of the concentration change used for inputs into Equation 3.

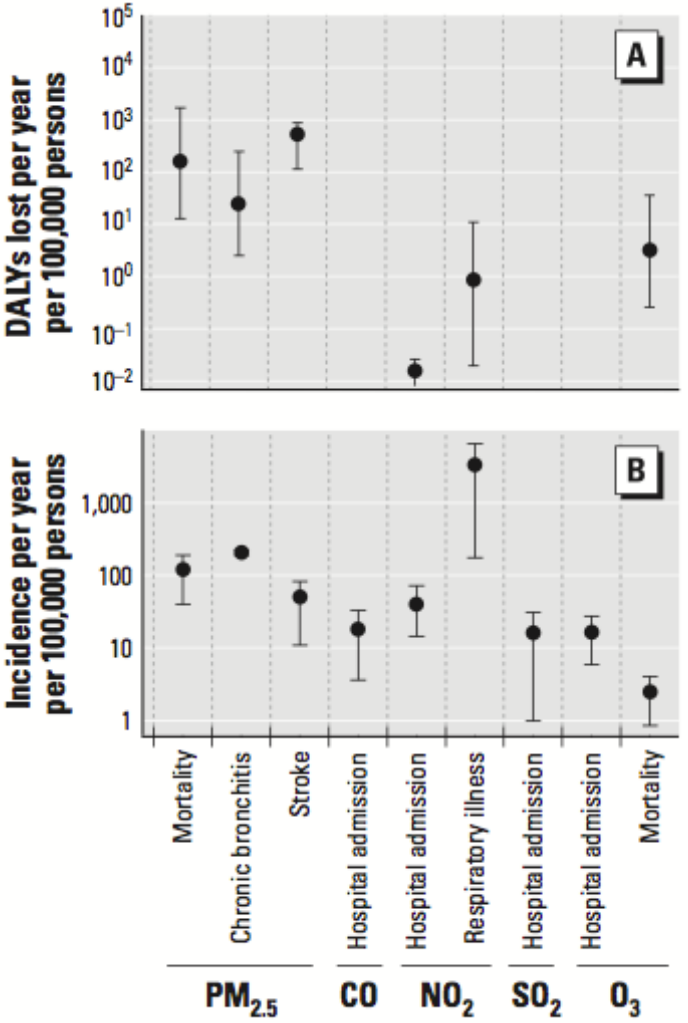
A Method to Estimate the Chronic Health Impact of Air Pollutants in U.S. Residences

Logue et al., *Environ Health Persp* **2012**

Intake-DALY approach

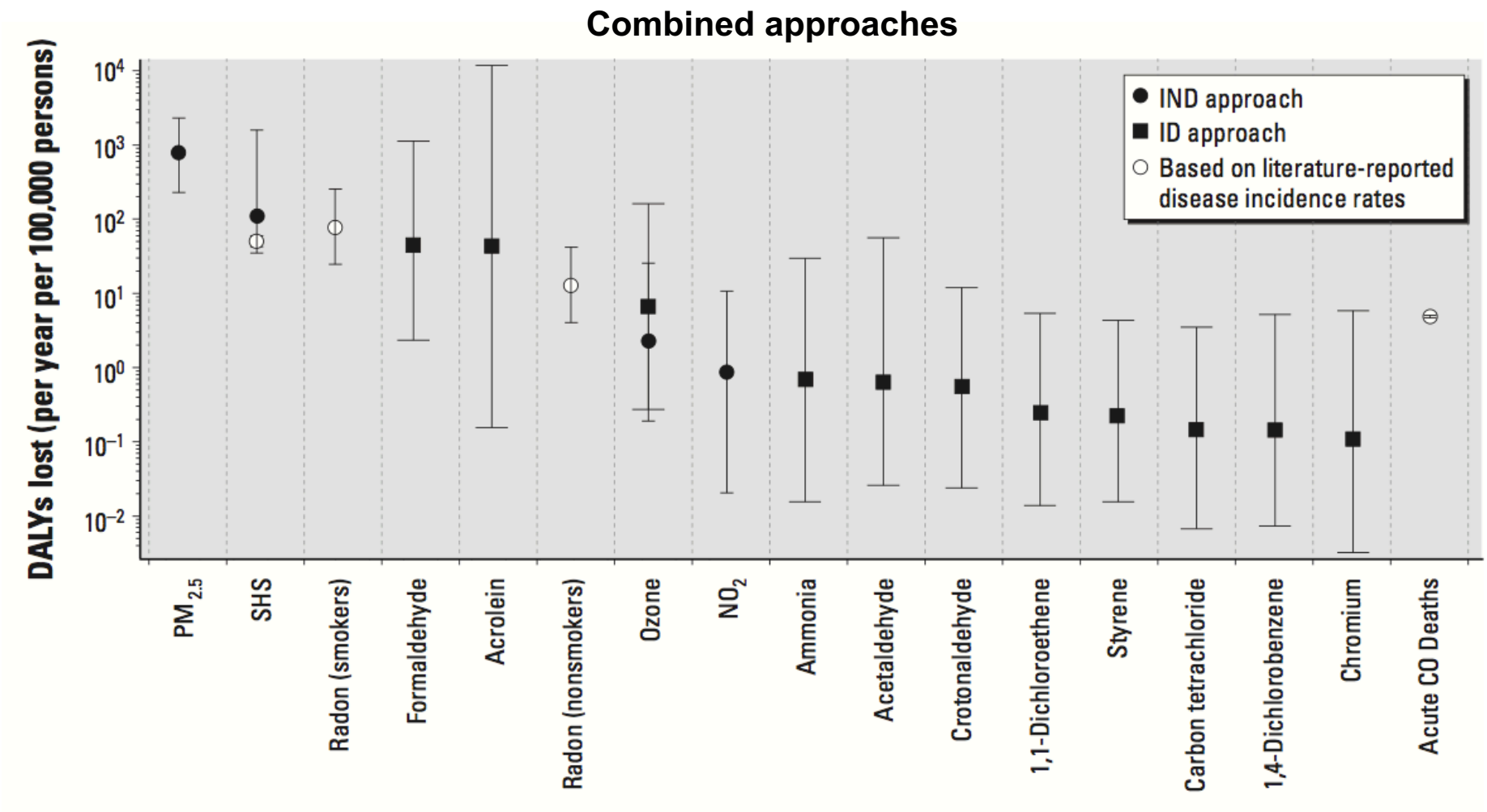


Intake-incidence-DALY approach



A Method to Estimate the Chronic Health Impact of Air Pollutants in U.S. Residences

Logue et al., *Environ Health Persp* **2012**



- Residential indoor air exposures account for **~5-14%** of the non-communicable/non-psychiatric **U.S. disease burden**

DIRECT INDOOR AIR EPIDEMIOLOGY STUDIES

*Not an exhaustive list; just some key examples

Direct indoor air epidemiology studies

- Fewer in number compared to outdoor air
- (Much) smaller sample sizes than outdoor air
- Inconsistent methodological approaches
- Still useful for showing associations in human populations

Gas stoves

Association between gas cooking and respiratory disease in children

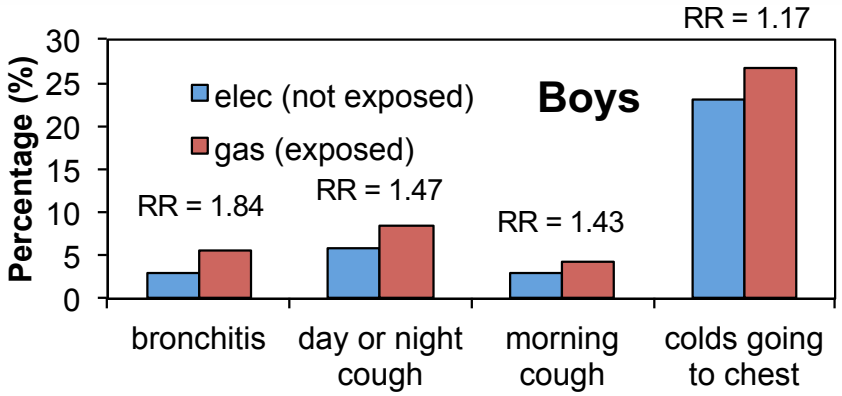
Melia et al., *British Medical Journal* **1977**, 2, 149-152

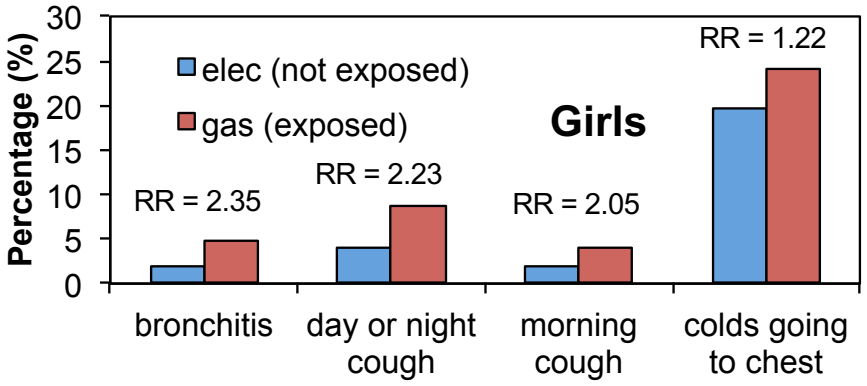
- Four-year longitudinal study of the prevalence of respiratory symptoms and disease in almost 6000 6-11 year old school children
  - Children from homes in which gas was used for cooking were found to have more cough, “colds going to the chest,” and bronchitis than children from homes where electricity was used

TABLE I—*Prevalence (%) of respiratory symptoms and diseases during last 12 months in boys and girls according to type of fuel used for cooking in the home*

Symptoms and diseases	Boys			Girls		
	Electricity	Gas	P*	Electricity	Gas	P*
Bronchitis	3·1	5·7	<0·001	2·0	4·7	<0·001
Day or night cough	5·8	8·5	<0·007	3·9	8·7	<0·001
Morning cough	3·0	4·3	<0·07	2·0	4·1	<0·001
Colds going to chest	23·0	26·8	<0·02	19·8	24·1	<0·006
Wheeze	10·3	11·2	≈0·5	5·7	8·6	<0·005
Asthma	1·8	2·7	≈0·2	1·0	1·6	≈0·2
No of children	1648	1274		1556	1280	

*Probability value for difference between prevalence rates, χ^2 test.





Respiratory Symptoms in Children and Indoor Exposure to Nitrogen Dioxide and Gas Stoves

Gas stoves

Garrett et al., *Am. J. Respir. Crit. Care. Med.* **1998**, 158, 891-895

- NO_2 measured in 80 homes in Australia using passive samplers
  - 148 children 7-14 years old were recruited (53 had asthma)
  - Indoor median NO_2 concentrations were 6 ppb (max 128 ppb)
  - Respiratory symptoms were more common in children exposed to a gas stove (OR = 2.3) after adjustments for parental allergy, parental asthma, and gender
  - NO_2 exposure was a marginal risk factor for respiratory symptoms
    - Gas stove was still a risk factor after accounting for NO_2
    - What does that mean?

Respiratory Symptom	% of Children	Gas Stove Exposure		Bedroom NO_2	
		OR*	95% CI	OR*	95% CI
Cough	59	2.25	1.13–4.49	1.47	0.99–2.18
Shortness of breath	31	1.49	0.72–3.08	1.23	0.92–1.64
Waking short of breath	17	1.01	0.42–2.45	1.04	0.71–1.53
Wheeze	24	1.79	0.80–3.99	1.15	0.85–1.54
Asthma attacks	23	1.73	0.77–3.90	1.06	0.77–1.46
Chest tightness	13	3.11	1.07–9.05	1.12	0.81–1.56
Cough in the morning	24	1.42	0.63–3.19	1.25	0.92–1.69
Chest tightness in morning	14	1.10	0.42–2.88	1.32	0.95–1.84

* Adjusted for parental asthma, parental allergy, and sex.

Gas stoves

A cross-sectional study of the association between ventilation of gas stoves and chronic respiratory illness in U.S. children enrolled in NHANESIII

Kile et al., *Environmental Health* **2014**, 13, 71

- The Third National Health and Nutrition Examination Survey was used to identify U.S. children aged 2–16 years with information on respiratory outcomes (asthma, wheeze, and bronchitis) who lived in homes where gas stoves were used in the previous 12 months and whose parents provided information on ventilation. Logistic regression models evaluated the association between prevalent respiratory outcomes and ventilation in homes that used gas stoves for cooking and/or heating. Linear regression models assessed the association between spirometry measurements and ventilation use in children aged 8–16 years.

Table 2 Adjusted Odds ratios and 95% confidence intervals for the association between respiratory illnesses in children aged 2–16 years who live in households that use gas stove with ventilation compared to households that use gas stoves without ventilation (Model 1)

	Ever diagnosed with asthma[a] (N = 5,745)		Wheeze in past 12 months[b] (N = 5,744)		Ever diagnosed with bronchitis[c] (N = 7,255)	
Ventilation of gas stove	**No. cases**	**OR (95% CI)**	**No. cases**	**OR (95% CI)**	**No. cases**	**OR (95% CI)**
No	*269*	1 Ref.	*561*	1 Ref.	*188*	1 Ref.
Yes	*224*	0.64 (0.43, 0.97)*	*458*	0.60 (0.42, 0.86)*	*128*	0.60 (0.37, 0.95)*

*P-value <0.05.

[a]Adjusted for age group, sex, parental history of asthma or hay fever, and furry or feathery pets in the house, household income < $20,000, and BMI percentiles for age.

[b]Adjusted for age group, parental history of asthma or hay fever, furry or feathery pets in the house, indoor tobacco smoke, race-ethnicity, household income < $20,000, and BMI percentile for age.

[c]Adjusted for age group, parental history of asthma or hay fever, indoor tobacco smoke, race-ethnicity, household income < $20,000, and census region.

"One-second forced expiratory volume (FEV_1) and FEV_1/FVC ratio was also higher in girls who lived in households that used gas stoves with ventilation compared to households that used gas stoves without ventilation."

Association of domestic exposure to volatile organic compounds with asthma in young children

Rumchev et al., *Thorax* **2004**, 59, 746-751

- Population based case-control study conducted in Perth, Australia
  - Children 6 months to 3 years of age (cases = 88; controls = 104)
  - Cases had asthma; controls did not
  - Housing questionnaires were given and indoor VOCs were measured

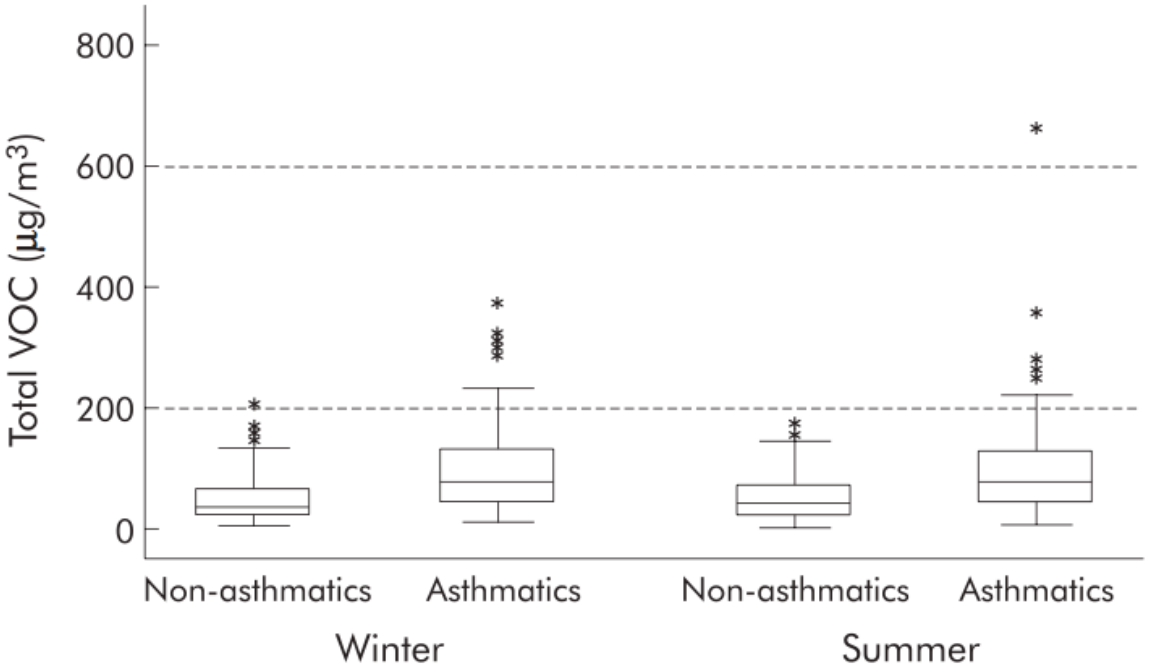


Figure 1 Seasonal differences in exposure levels to total volatile organic compounds (VOCs, µg/m^3) for asthmatic and non-asthmatic children.

Association of domestic exposure to volatile organic compounds with asthma in young children

Rumchev et al., *Thorax* **2004**, 59, 746-751

- Cases had significantly higher VOC levels than controls ($p < 0.01$)
  - Highest odds ratios were benzene > ethylbenzene > toluene

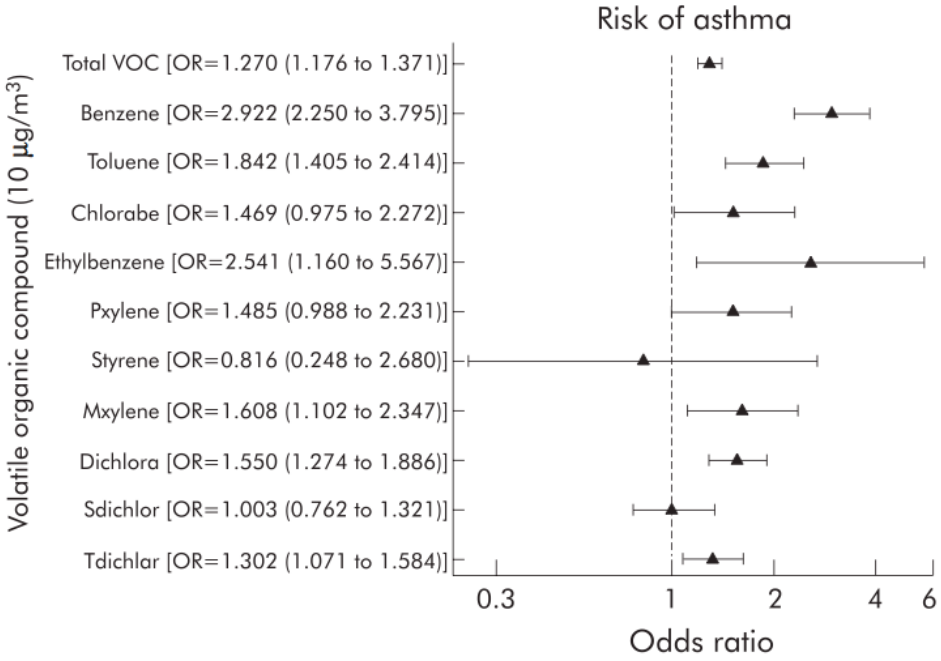


Figure 3 Adjusted odds ratio with ±95% confidence intervals for the risk of asthma with each 10 mg increase in exposure to VOCs.

Exposure-response curve

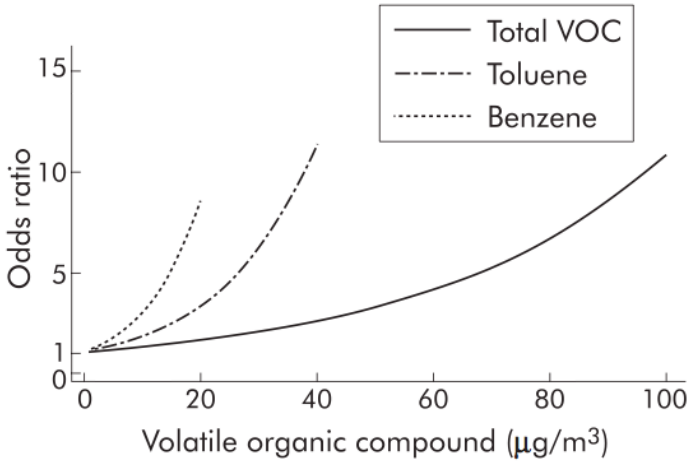


Figure 2 Asthma in young children associated with exposure to indoor volatile organic compounds (µg/m^3): odds ratios adjusted for age, sex, atopy, socioeconomic status, smoking indoors, air conditioning, house dust mites, and gas appliances.

Frequent use of chemical household products is associated with persistent wheezing in pre-school age children

Sherriff et al., *Thorax* **2005**, 60, 45-49

Use of cleaning products

- Frequency of use of 11 chemical based domestic products was determined via questionnaires completed by women during pregnancy
  - Given a "total chemical burden" score (TCB)
- Four wheezing patterns were defined for the period from baby's birth to 42 months of age (never, transient early, persistent, late onset)
- 13971 children tracked; completely data for 7019 children

> Fifteen product categories were included in the questionnaire and, from this initial list, we selected the 11 most frequently used (by at least 5% of the study sample). The products chosen (and the percentages of women using them) were: disinfectant (87.4%), bleach (84.8%), carpet cleaner (35.8%), window cleaner (60.5%), dry cleaning fluid (5.4%), aerosols (71.7%), turpentine/white spirit (22.6%), air fresheners (spray, stick or aerosol) (68%), paint stripper (5.5%), paint or varnish (32.9%), and pesticides/insect killers (21.2%). A simple score for frequency of use of each product was derived (0 = not at all, 1 = less than once a week, 2 = about once a week, 3 = most days, 4 = every day) and the scores for each product were summed to produce a total chemical burden (TCB) score for each respondent which could range from 0 (no exposure) to 55 (exposed to all 11 products daily).

Frequent use of chemical household products is associated with persistent wheezing in pre-school age children

Sherriff et al., *Thorax* **2005**, 60, 45-49

Use of cleaning products

Table 1 Unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for wheezing phenotypes* (transient early wheeze, persistent wheeze, and late onset wheeze (0–42 months)) according to total chemical burden (TCB) score measured during pregnancy (continuous)

Wheezing phenotype	% (N)	Unadjusted OR (95% CI) (N=7019)	Unadjusted p value	Adjusted OR** (95% CI) (N=5691)	Adjusted p value
Never wheezed	71.2 (5001)	1 (reference)		1 (reference)	
Transient early wheeze	19.1 (1340)	1.02 (1.00 to 1.03)	0.04	1.01 (0.99 to 1.02)	0.6
Persistent wheeze	6.2 (432)	1.08 (1.05 to 1.11)	<0.0001	1.06 (1.03 to 1.09)	0.0001
Late onset wheeze	3.5 (246)	1.02 (0.99 to 1.05)	0.2	1.02 (0.98 to 1.06)	0.3

*Never wheezed 0–42 months. Transient early wheeze: wheeze 0–6 months and no wheeze 6–42 months. Persistent wheeze: wheeze 6–18 months, 18–30 months and 30–42 months. Late onset wheeze: wheeze onset 30–42 months.
**Adjusted for weekend exposure to environmental tobacco smoke at 6 months, maternal smoking during pregnancy, maternal history of asthma, maternal parity, crowding in the home, sex, contact with pets, damp housing, maternal age at delivery, maternal educational attainment, housing tenure, hours mother worked outside home, month of returning chemical usage questionnaire, and duration of breastfeeding.

Table 2 Unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for wheezing phenotypes* (transient early wheeze, persistent wheeze, and late onset wheeze (0–42 months)) according to total chemical burden (TCB) score measured during pregnancy (bottom decile versus top decile)

Wheezing phenotype	Bottom decile of TCB % (N)	Top decile of TCB % (N)	Unadjusted OR (95% CI) (N=7019)	Unadjusted p value	Adjusted OR** (95% CI) (N=5691)	Adjusted p value
Never wheezed	74.9 (603)	66.9 (338)	1 (reference)		1 (reference)	
Transient early wheeze	18.8 (151)	19.0 (96)	1.13 (0.90 to 1.50)	0.4	0.94 (0.60 to 1.40)	0.7
Persistent wheeze	4.0 (32)	10.1 (51)	2.84 (1.79 to 4.51)	<0.0001	2.30 (1.20 to 4.39)	0.012
Late onset wheeze	2.4 (19)	4.0 (20)	1.88 (0.99 to 3.57)	0.05	2.02 (0.80 to 5.15)	0.14

*Never wheezed 0–42 months. Transient early wheeze: wheeze 0–6 months and no wheeze 6–42 months. Persistent wheeze: wheeze 6–18 months, 18–30 months and 30–42 months. Late onset wheeze: wheeze onset 30–42 months.
**Adjusted for weekend exposure to environmental tobacco smoke at 6 months, maternal smoking during pregnancy, maternal history of asthma, maternal parity, crowding in the home, sex, contact with pets, damp housing, maternal age at delivery, maternal educational attainment, housing tenure, hours mother worked outside home, month of returning chemical usage questionnaire, and duration of breastfeeding.

The Use of Household Cleaning Sprays and Adult Asthma

Zock et al., *Am. J. Respir. Crit. Care. Med.* **2007**, 176, 735-741

Use of cleaning products

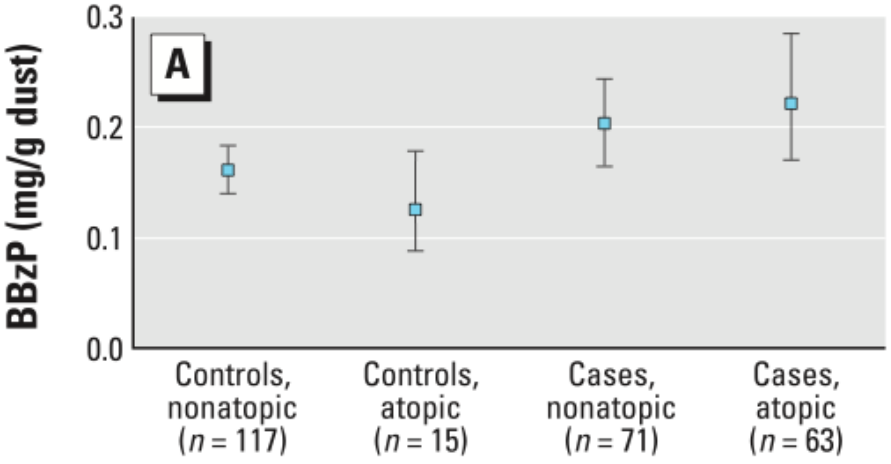
- Identified 3503 people in 10 countries who do the cleaning in their homes and who were free of asthma at the beginning of the study
- Frequency of use of 15 types of cleaning products was obtained by interview
- Tracked incidence of asthma
- Use of cleaning sprays at least weekly (42% of participants) was associated with asthma symptoms or medication use (RR = 1.49) and wheeze (RR = 1.39)
  - Asthma was higher among those using sprays at least 4 days per week (RR = 2.11)
  - Highest risks for glass-cleaning, furniture, and air-freshener sprays
  - Non-spray-form products were not associated

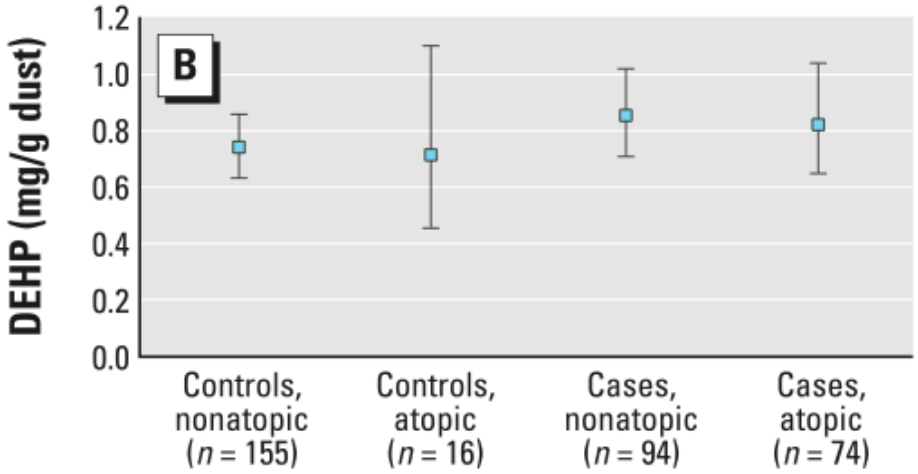
SVOCs and asthma/allergy

The Association between Asthma and Allergic Symptoms in Children and Phthalates in House Dust: A Nested Case–Control Study

Bornehag et al., *Environ. Health Perspect.* **2004**, 112, 1393-1397

- Cohort of 10852 children
  - 198 cases with persistent allergic symptoms
  - 202 controls without symptoms
- Measured phthalate concentrations in house dust
- BBzp (butyl benzyl phthalate) was higher in cases than controls
  - Associated with rhinitis (stuffy/runny nose) and eczema (inflammation of skin)
- DEHP was associated with asthma





SVOCs and thyroid function

Relationship between Urinary Phthalate and Bisphenol A Concentrations and Serum Thyroid Measures in U.S. Adults and Adolescents from the National Health and Nutrition Examination Survey (NHANES) 2007–2008

- Analysis of urinary biomarker data of exposure to phthalates (DEHP, DBP) and BPA for 1346 adults and 329 adolescents using the National Health and Nutrition Examination Survey (NHANES)
  - Compared to serum thyroid measures
- Found significant relationships between phthalates (and possibly BPA) and altered thyroid hormones
  - These hormones play important roles in fetal and child growth and brain development, as well as metabolism, energy balance, and other functions in the nervous, cardiovascular, pulmonary, and reproductive systems

Meeker and Ferguson, *Environ Health Perspectives* **2011**

Ventilation rates and health

Association between ventilation rates in 390 Swedish homes and allergic symptoms in children

Bornehag et al., *Indoor Air* **2005**

- Same cases (198) and controls (202) from before
- Compared symptoms and diagnoses to AER measurements
  - Cases had significantly **lower** ventilation rates

Table 3 Differences in mean ventilation rate between cases and controls in different groups of buildings

			P-value	
Type of buildings	Cases	Controls	*t*-test	Mann–Whitney *U*
Single-family houses (*n*)	161	172		
Mean ach in total building (*n*)	0.34 (161)	0.38 (169)	0.025	0.014
Ach in child's bedroom (*n*)	0.32 (158)	0.37 (166)	0.020	0.011
Chain houses (*n*)	12	11		
Mean ach in total building (*n*)	0.37	0.32	0.627	0.622
Ach in child's bedroom (*n*)	0.40	0.33	0.412	0.712
Multi-family houses (*n*)	25	19		
Mean ach in total building (*n*)	0.49 (25)	0.47 (18)	0.793	1.000
Ach in child's bedroom (*n*)	0.50 (23)	0.52 (17)	0.807	0.967
All types of building (*n*)	198	202		
Mean ach in total building (*n*)	0.36 (198)	0.39 (198)	0.126	0.053
Ach in child's bedroom (*n*)	0.34 (193)	0.38 (194)	0.099	0.068

Significant difference was ~14% lower ACH in cases than controls

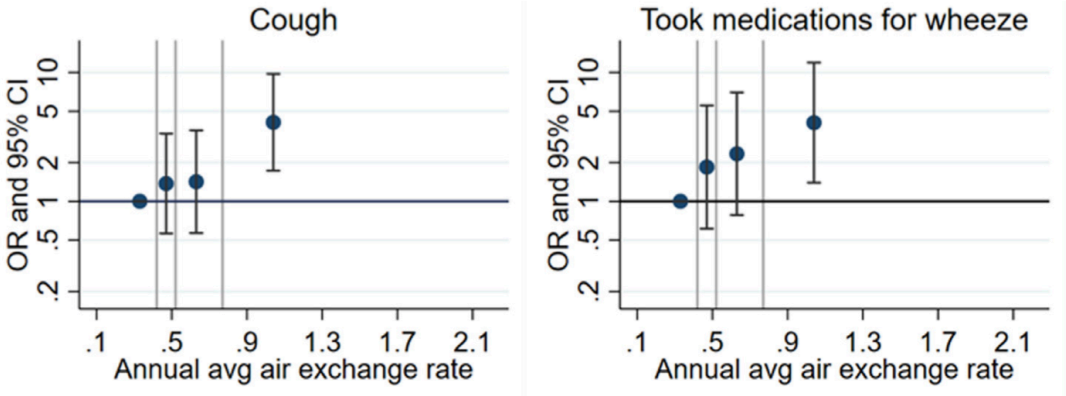
Ventilation rates and health

Relationships between home ventilation rates and respiratory health in the Colorado Home Energy Efficiency and Respiratory Health (CHEER) study

Elizabeth J. Carlton[a,*], Kelsey Barton[a], Prateek Man Shrestha[b], Jamie Humphrey[b], Lee S. Newman[a,c], John L. Adgate[a], Elisabeth Root[d], Shelly Miller[b]

Carlton et al., *Environmental Research* **2019**

- Cross-sectional study (n=302) of 216 non-smoking, low-income homes
- Blower door test conducted; results used to estimate annual average AER
- Respiratory health assessed using a structured questionnaire
- Residents in homes with higher annual average AER were more likely to report chronic cough, asthma and asthma-like symptoms
  - The association between AAER and asthma-like symptoms was stronger for households located in areas with high potential exposure to traffic related pollutants



HVAC systems and health

Risk factors in heating, ventilating, and air-conditioning systems for occupant symptoms in US office buildings: the US EPA BASE study

Mendell et al., *Indoor Air* **2008**

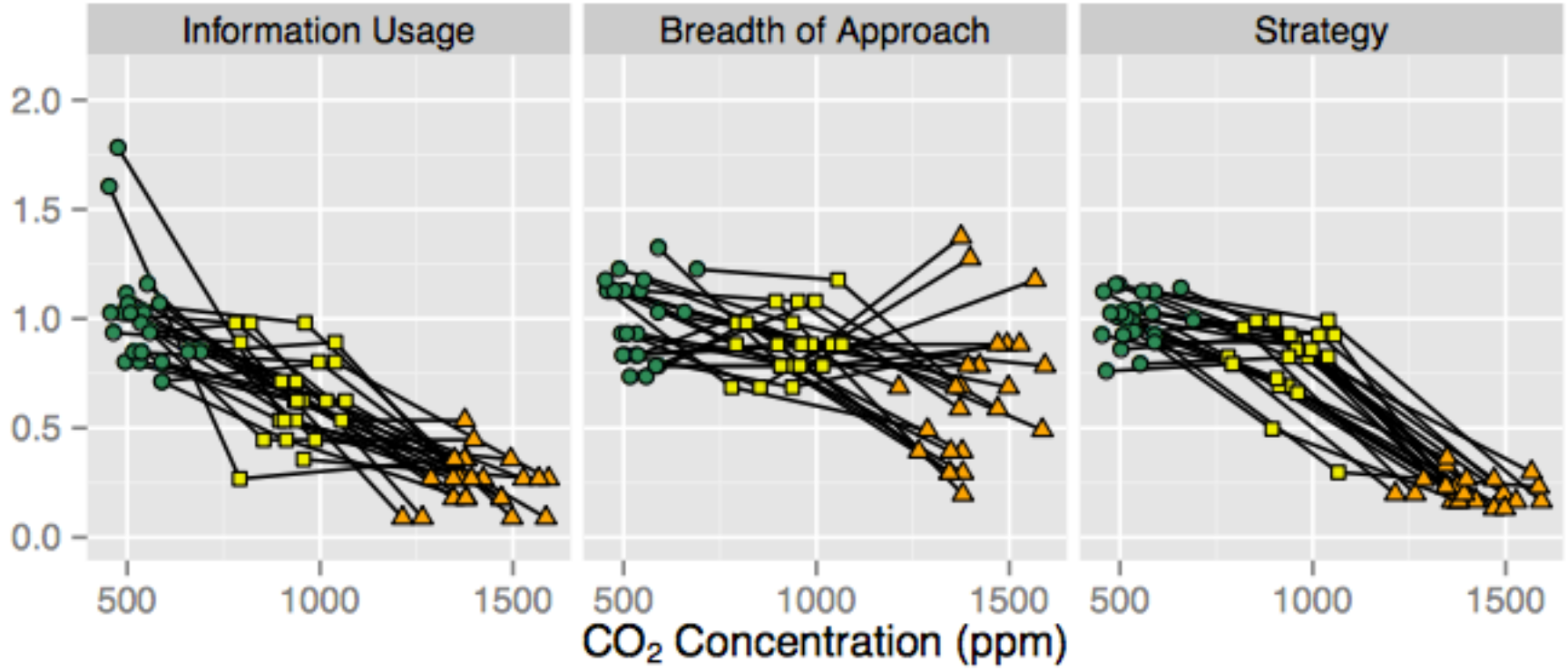
- 'Building-related symptoms' in office workers were assessed in 97 air-conditioned office buildings in the US
- A primary correlation between building symptoms and HVAC characteristics was:
  - Outdoor air intakes less than 60 m above ground level were associated with significant increases in most symptoms
  - For upper respiratory symptoms, OR for intake heights were:
    - <30 m: OR = 2.0
    - 30-60 m: OR = 2.7
    - Below ground: OR = 2.1
    - Above 60 m: OR = 1.0
  - Poorly maintained humidification systems and infrequent cleaning of cooling coils and drain pans were also associated
    - What does this suggest?

Ventilation, CO_2, and cognitive function

Satish et al **2012** *Environ Health Perspectives*

Ventilation, CO_2, and cognitive function

Scientists report a surprising link between indoor carbon dioxide levels and cognitive function



Allen et al **2016** *Environ Health Perspectives*

https://www.washingtonpost.com/news/energy-environment/wp/2015/10/27/why-your-office-air-could-be-crimping-your-productivity/

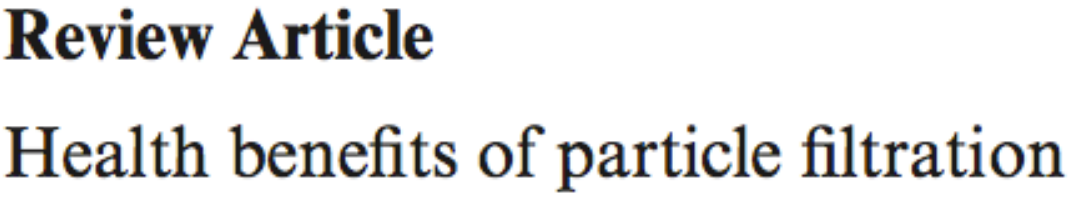
Photo from M.S. Waring and J.A. Siegel

AIR CLEANERS AND HEALTH

(Indirect) evidence of links between IAQ and health

Literature search

Seminal study:



Fisk **2013** *Indoor Air*

Reviewed 16 intervention studies (residential + commercial)

- Modest allergy and asthma improvements
- Some improvements in markers of future coronary events

Search terms for additional literature through 2018:

"indoor air"[All Fields] OR IAQ[All Fields] OR IEQ[All Fields] OR residence[All Fields] OR residential[All Fields] OR home[All Fields] OR house[All Fields] OR "household"[All Fields] AND ("air filter"[All Fields] OR "air cleaner"[All Fields] OR "air purifier"[All Fields] OR "filtration"[MeSH] OR "filtration"[All Fields]) OR "high efficiency particulate air filter"[All Fields] OR "HEPA filter"[All Fields]

Prioritized residential intervention studies (mostly since 2013)

Summarized in:
https://www.epa.gov/indoor-air-quality-iaq/air-cleaners-and-air-filters-home

Literature findings

- Two primary study approaches:

1. Residential air cleaner use and respiratory health outcomes and/or changes in allergy or asthma symptoms in subjects with allergies or asthma
   - 5 from Fisk (2013) + 3 new studies

2. Residential air cleaner use and primarily cardiovascular health outcomes or markers of these health outcomes in subjects without allergies and asthma
   - 4 from Fisk (2013) + 7 new studies

Literature findings: New studies

Table 1. Three additional studies targeting allergy and asthma outcomes

Reference	Subjects	Air cleaner
Bernstein et al. 2006	19 asthmatic children	220 CADR in bedroom + living room
Xu et al. 2006	30 asthmatic children	150 CADR + OA ventilation in bedroom
Park et al. 2017	16 allergic/asthmatic children	600/450 CADR (HEPA + carbon) in living/bed

CADR = Clean Air Delivery Rate (CFM), HEPA = High Efficiency Particulate Air, OA = Outdoor Air

Table 2. Seven additional studies targeting primarily cardiovascular outcomes

Reference	Subjects	Air cleaner
Karottki et al. 2013	48 elderly adults	HEPA (unknown CADR) in bed+living rooms
Chen et al. 2015	35 university students	Central filter (Filtrete) in living area
Kajbafzadeh et al. 2015	83 healthy adults	300/150 CADR (HEPA) in living/bed rooms
Padró-Martinez et al. 2015	20 non-smoking adults	MERV 17 (+170 cfm OA) in living rooms
Chuang et al. 2017	200 healthy adults	MPR 1000 in living/bed window AC units
Shao et al. 2017	35 elderly adults	215/177 CADR (HEPA+carbon) in living/bed
Cui et al. 2018	70 healthy adults	100 CADR (HEPA+carbon) in dorm living area

Literature findings: New studies

- Fisk WJ. 2013. *Indoor Air* 23(5):357-368
- Bernstein JA et al 2006. *Journal of Asthma* 43(4):255-262
- Xu Y et al 2010. *Building and Environment* 45:330-337
- Park HK et al 2017. *Journal of Asthma* 54(4):3441-3446
- Karottki DG et al 2013. *Environmental Health* 12:116
- Chen R et al 2015. *Journal of the American College of Cardiology* 65:2279-2287
- Kajbafzadeh M et al 2015. *Occupational and Environmental Medicine* 72:394-400
- Padró-Martinez L et al 2015. *Int J Environ Res Public Health* 12:7814-7838
- Chuang HC et al 2017. *Environment International* 106:91-96
- Shao D et al 2017. *Science of the Total Environment* 603-604:541-549
- Cui X et al 2018. *Environment International* 114:27–36

Updated health effects review: Methodology

Evaluation criteria

- Subject information
- Type of building
- Exposure focus
- Filter location and type
- Intervention period
- Reduction in exposures
- Change in allergy/asthma symptoms (if appropriate)
- Change in objective health functions
- Assessment of study strength
- Author(s) main conclusions

Updated health effects review: Allergies and asthma

Study	Brehler et al. (2003)	Francis et al. (2003)	Bernstein et al. (2006)	Sulser et al. (2009)
Subjects	44 adults with allergies and/or asthma	30 adults allergic to cats or dog allergen	19 mold-sensitized asthmatic children, age 5 to 17 years	30 asthmatic children sensitive to pet allergen
Type of building	Homes (24 rural, 20 urban)	Homes with cats or dogs	Homes with central forced air HVAC systems	Homes with high cat or dog allergen levels in dust
Exposures focus	General particles, pollens	Pet allergen	Allergens in dust, bacterial, and fungal counts in air and dust	Pet allergen
First filter location, type, and CADR	Bedroom outdoor air supply (fresh air, no filter)	Bedroom (HEPA, unknown CADR)	In-duct central HVAC (CREON2000 UVGI with HEPA pre-filter)	Bedroom (220 cfm)
Second filter location, type, and CADR	n/a	Living room (HEPA, unknown CADR)	n/a	Living room (220 cfm)
Gas-phase filtration	No	No	No	No
Intervention period	2 weeks	12 months	8 weeks	12 months
Reduction in exposures	Not reported	• SS and substantial reductions in airborne cat and dog allergen in both groups • Reductions in intervention group not SS relative to reductions in control group	• Small but not SS reduction in mold and bacterial counts in indoor air with UVGI unit versus placebo • No SS difference in allergens or molds in house dust samples	No SS change in cat and dog allergen concentration in dust
Change in allergy and asthma symptoms	Subjects with seasonal allergy: • Nose[a] ↓ (30%) ↔ • Eyes[a] ↓ (42%) ↔ • Lung ↔ Subjects with perennial allergy: • Nose ↔ • Eyes ↔ • Lung ↔	n/a	First treatment period only: • Asthma symptoms ↓ • Asthma medication use ↓ Not in Fisk (2013)	Nasal ↓ Nocturnal ↓ Pediatric quality of life score ↔
Change in objective health outcomes	• Peak expiratory flow (PEF, a measure of how fast a person can exhale) in morning ↓ (5%) • PEF in daytime ↔	• Bronchial hyper-reactivity and/or asthma treatment requirements ↓ • Forced expiratory volume (FEV, how much air a person can exhale during a breath) ↔ • Forced vital capacity (total amount of air exhaled during an FEV test) ↔	Both treatment periods: • Peak expiratory flow (PEF) rate variability ↓ (~2% mean; ~59% median)	• Forced expiratory volume (FEV) ↔ • Eosinophil cationic protein (inflammation marker) ↔ • Non-SS trend toward improved bronchial hyper-responsiveness
Assessment of study strength	Strong (crossover, placebo, randomized order of exposure)	Moderate (random assignment to intervention vs. control group, no placebo)	Moderate (random assignment, placebo, crossover design), but small sample size	Strong (control group with placebo, random assignment to groups)
Author(s) main conclusion(s)	Recommends fresh air filtration systems in bedrooms.	"Small but significant improvement in combined asthma outcome."	"Central UV irradiation was effective at reducing airway hyper-responsiveness manifested as peak expiratory flow rate variability and some clinical symptoms."	"Although HEPA air cleaners retained airborne pet allergens, no effect on disease activity...was observed."

Updated health effects review: Allergies and asthma

Study	Xu et al. (2010)[a]	Butz et al. (2011)	Lanphear et al. (2011)	Park et al. (2017)[e]
Subjects	30 children with asthma	85 children with asthma[b]	215 children with asthma	16 children with asthma and/or allergic rhinitis
Type of building	Homes in New York state	Homes with smokers	Homes with smokers	Homes in California
Exposures focus	General particles and gases	Environmental tobacco smoke	Environmental tobacco smoke	General particles
First filter location, type, and CADR	Bedrooms (HEPA, ~150 cfm, with ~3 air changes per hour of outdoor air ventilation)	Bedroom (HEPA, 225 cfm)	Bedroom (HEPA, 220 cfm)	Living room (HEPA with activated carbon, ~600 cfm)
Second filter location, type, and CADR	n/a	Living room (HEPA, 225 cfm)	Main activity room (HEPA, 220 cfm)	Bedroom (HEPA with activated carbon, ~450 cfm)
Gas-phase filtration	No	Yes (activated carbon)	Yes (activated carbon and potassium permanganate zeolite)	Yes (activated carbon)
Intervention period	6 weeks	6 months	12 months	12 weeks
Reduction in exposures	• 72% ($PM_{2.5-10}$) • 59% (TVOC)	• Intervention group: SS 19.9 and 8.7 µg/m³ (59% and 46%) decreases in $PM_{2.5}$ and PM_{10}, respectively versus control group • Control group: 3.5 and 2.4 µg/m³ (9% and 14%) increases in $PM_{2.5}$ and PM_{10}, respectively • No SS changes in air nicotine or urine cotinine concentrations	• SS 25% reduction in particle counts >0.3 µm in intervention group relative to 5% reduction in control group • No SS reductions in particle counts >5 µm or airborne nicotine	43% ($PM_{2.5}$)
Change in allergy and asthma symptoms	n/a	• Symptom-free days[c] ↓ (10%) • Slow activity days ↔ • Nocturnal cough ↔ • Wheeze ↔ • Tight chest ↔	• Asthma symptoms ↔	• Asthma control test scores ↑ (~45%) • Nasal symptom scores ↓ (~30%)
Change in objective health outcomes	• Peak expiratory flow (PEF) ↑ • Exhaled breath nitrate concentration (pulmonary inflammation marker) ↓ • Exhaled breath condensate pH (pulmonary inflammation marker) ↑	n/a	• Unscheduled asthma-related visits to a healthcare provider ↓ (25%) • Exhaled nitric oxide (inflammation indicator) ↔ • Medication use ↔	• Peak expiratory flow (PEF) ↑ (~100%)
Assessment of study strength	Weak (all participants received crossover intervention, with randomized different timings; effect size is difficult to interpret)	Moderate (random assignment to intervention vs. control group, no placebo)	Strong (control group with placebo, random assignment to groups)	Weak (randomized control and intervention groups, small sample size of 8 homes per group, no placebo, no crossover)
Author(s) main conclusion(s)	"Air cleaning in combination with ventilation can effectively reduce symptoms for asthma sufferers."[d]	Air cleaners reduce particles and symptom-free days but do not prevent exposure to secondhand smoke.	Air cleaners promising "as part of multi-faceted strategy to reduce asthma morbidity."	"Reducing indoor $PM_{2.5}$ with air purifiers may be an effective means of improving clinical outcomes in patients with allergic diseases."

Not in Fisk (2013)

Summary of allergies/asthma intervention studies

- 8 intervention studies investigated air cleaner use and respiratory health outcomes and/or changes in allergy or asthma symptoms in subjects with allergies or asthma
  - 5 from Fisk (2013) and 3 new studies since then
    - 6 investigated portable air cleaners (mostly HEPA)
    - 1 investigated a bedroom outdoor air supply w/out filter
    - 1 investigated central in-duct UVGI unit

- All 8 studies reported statistically-significant improvements in at least one objective or self-reported health endpoint
  - Peak expiratory flow, bronchial inflammation markers, medication use, or symptoms scores

- Magnitudes of improvements typically modest

Updated health effects review: Non-allergies/asthma

Study	Bräuner et al. (2008)	Allen et al. (2011)	Lin et al. (2011)	Weichenthal et al. (2013)
Subjects	41 healthy non-smoking adults age 60–75	45 adults	60 healthy non-smoking young adults (students)	37 adults and children, 6 with asthma
Type of building	Urban homes within 350 m of a major road in Denmark	25 homes in a small city in Canada	Homes in Taiwan	First Nations homes in Canada, most with smoking
Exposures focus	General particles	Wood smoke	General particles	General particles, tobacco smoke
First filter location, type, and CADR	Bedroom (HEPA, ~320 cfm)	Bedroom of each home (HEPA, 150 cfm)	Central HVAC filter (3M Filtrete)	Main living area (224 cfm)
Second filter location, type, and CADR	Living room (HEPA, ~320 cfm)	Living room (HEPA, 300 cfm)	n/a	n/a
Gas-phase filtration	No	No	No	No
Intervention period	2 days	1 week	4 weeks	1 week
Exposure concentration without treatment	12.6 μg/m³ ($PM_{2.5}$ geometric mean) 9.4 μg/m³ ($PM_{2.5-10}$ geometric mean) 10,016 cm⁻³ (count 10–700 nm)	11.2 μg/m³ ($PM_{2.5}$ mean)	22.8 ± 12.2; 24.5 ± 13.0 μg/m³ ($PM_{2.5}$ mean)	49.0 μg/m³ (PM_{10}) 42.5 μg/m³ ($PM_{2.5}$) 37.5 μg/m³ (PM_1)
Reduction in exposures	63% ($PM_{2.5}$ geometric mean) 51% (PM_{10} geometric mean) 68% (count 10–700 nm)	60% $PM_{2.5}$ 74% levoglucosan (wood smoke marker)	~20% reduction in $PM_{2.5}$	54% (PM_{10}) 61% ($PM_{2.5}$) 62% (PM_1)
Change in objective health outcomes	Microvascular function (coronary event predictor) ↓ (8%) Hemoglobin ↓ (1%) Inflammation biomarker ↔ Biomarker of coagulation ↔	Reactive hyperemia index (coronary event predictor) ↓ (9%) C-reactive protein (inflammation marker) ↓ (33%) Oxidative stress ↔	Systolic blood pressure ↓ (11%) Diastolic blood pressure ↓ (7%) Heart rate ↓ (7%)	Systolic blood pressure ↓ (7%) Diastolic blood pressure ↓ (6%) Forced expiratory flow (PEF) ↓ (6%) Forced vital capacity ↔ Peak expiratory flow ↓ (8%) Reactive hyperemia index (coronary event predictor) ↔
Assessment of study strength	Strong (blinded, placebo-controlled intervention, within-subject, randomized order of exposure	Strong (crossover, placebo, randomized order of exposure)	Weak (intervention periods always followed periods without intervention)	Strong (randomized double blind crossover with placebo)
Author(s) main conclusion(s)	Filtration of recirculated air may be a feasible way of reducing the risk of cardiovascular disease.	Predictors of cardiovascular morbidity can be favorably influenced by reducing particles with air cleaners.	Air filtration can reduce indoor $PM_{2.5}$ concentrations and modify the effect of $PM_{2.5}$ on blood pressure and heart rate in a healthy, young population.	Reducing indoor PM may contribute to improved lung function in First Nation communities.

Updated health effects review: Non-allergies/asthma

Study	Karottki et al. (2013)[a]	Chen et al. (2015)[a]	Kajbafzadeh et al. (2015)[a]	Padró-Martínez et al. (2015)[a]
Subjects	48 elderly nonsmoking adults	35 healthy university students	83 healthy adults	20 non-smoking adults
Type of building	27 homes in Denmark	Dormitories in Shanghai, China	Homes in Vancouver, British Columbia, Canada	Public housing units within 200 m of major interstate in Somerville, Massachusetts
Exposures focus	General particles	Indoor particles of outdoor origin	Traffic and woodsmoke particles	Traffic-related and general indoor particles
First filter location, type, and CADR	Living room (HEPA, unknown CADR)	Center of the room (Filtrete, 141, 116, and 97 cfm for pollen, dust, and smoke)	Living room (HEPA, 300 cfm for smoke)	Window mounted in living rooms (MERV 17, 170 cfm with outdoor air ventilation)
Second filter location, type, and CADR	Bedroom (HEPA, unknown CADR)	n/a	Bedroom (HEPA, 150 cfm for smoke)	n/a
Gas-phase filtration	No	No	No	No
Intervention period	2 weeks	2 days	1 week	3 weeks
Exposure concentration without treatment	8 μg/m^3 ($PM_{2.5}$ median) 7,669 cm^{-3} (count)	96.2 μg/m^3 ($PM_{2.5}$ mean)	7.1 μg/m^3 ($PM_{2.5}$ mean)	11,660 cm^{-3} (count, mean of medians)
Reduction in exposures	~50% ($PM_{2.5}$) ~30% (10–300 nm particle number)	57% ($PM_{2.5}$)	40% ($PM_{2.5}$)	47% (7 nm to 3 μm number concentrations, or PNC)
Change in objective health outcomes	Microvascular function ↑[a] ↔ Lung function ↔ Biomarkers of systemic inflammation ↔ Not in Fisk (2013)	Circulatory inflammatory markers: • Monoctyle chemoattractant protein-1 ↓ (18%) • Interleukin-1β ↓ (68%) • Myeloperoxidase ↓ (33%) Circulatory coagulation markers: • Soluble CD40 ligand ↓ (65%) Systolic blood pressure ↓ (3%) Diastolic blood pressure ↓ (5%) Fractional exhaled nitrous oxide ↓ (17%) Several other biomarkers of inflammation, coagulation, vasoconstriction or lung function ↔	Biomarkers of systemic inflammation: • C reactive protein ↓[b] • Interleukin-6 ↔ • Band cells ↔ Microvascular endothelial function ↔ Reactive hyperaemia index ↔	Biomarkers of systemic inflammation and coagulation: • Interleukin-6 (IL-6) ↑ • C reactive protein ↔ • Tumor necrosis factor alpha-receptor II (TNF-RII) ↔ • Fibrinogen ↔ Systolic blood pressure ↔ Diastolic blood pressure ↔
Assessment of study strength	Strong (randomized, double-blind, crossover intervention)	Strong (randomized, double-blind crossover with placebo)	Strong (randomized, single-blind crossover with placebo)	Moderate (randomized, double-blind crossover with placebo; small sample sizes)
Author(s) main conclusion(s)	"Substantial exposure contrasts in the bedroom" observed.	The study "demonstrated clear cardiopulmonary benefits of indoor air purification among young, healthy adults in a Chinese city with severe ambient particulate air pollution."	The "association between C-reactive protein and indoor $PM_{2.5}$ among healthy adults in traffic-impacted areas is consistent with the hypothesis that traffic-related particles (even at low concentrations) play an important role in the cardiovascular effects of the urban PM mixture."	"HEPA filtration remains a promising, but not fully realized intervention." Associations between decreased PNC and increased IL-6 could be due to confounding factors, interference with anti-inflammatory medication use, or exposure misclassification due to time-activity patterns.

Updated health effects review: Cardiovascular

Study	Chuang et al. (2017)[d]	Shao et al. (2017)[d]	Cui et al. (2018)[e]
Subjects	200 healthy adults aged 30 to 65 years	35 elderly adults	70 non-smoking healthy adults aged 10 to 26 years
Type of building	Homes in Taipei	Homes in Beijing	Homes in a Shanghai suburb
Exposures focus	General particles and gases	General particles (much from outdoors)	General particles
First filter location, type, and CADR	Living room (3M Filtrete MPR 1000/MERV 11 in window air-conditioners)	Living room (Philips AC4374, HEPA and activated carbon with CADR of 215 cfm)	Living area (mostly dorms) (Amway Atmosphere, HEPA, and activated carbon with airflow rate of 100 cfm)
Second filter location, type, and CADR	Master and guest bedrooms (3M Filtrete MPR 1000/MERV 11 in window air-conditioners)	Bedroom (Philips AC4016, HEPA and activated carbon with CADR of 177 cfm)	n/a
Gas-phase filtration	No	Yes	Yes
Intervention period	1 year	2 weeks	1 day (overnight)
Exposure concentration without treatment	• 21.4 μg/m³ ($PM_{2.5}$ mean) • 1.22 ppm (TVOC mean)	60 μg/m³ ($PM_{2.5}$ mean)	• 33.2 μg/m³ ($PM_{2.5}$ mean) • 5938 #/cm³ (count mean)
Reduction in exposures	• ~40% ($PM_{2.5}$ mean) • ~65% (TVOC mean)	~60% ($PM_{2.5}$ mean)	• ~72% ($PM_{2.5}$ mean) • ~59% (PM count mean)
Change in objective health outcomes	• Systolic blood pressure ↓ (7%) • Diastolic blood pressure ↓ (6%) • High sensitivity-C-reactive protein (hs-CRP, a marker of inflammation) ↓ (50%) • 8-hydroxy-2'-deoxyguanosine (8-OHdG, a marker of oxidative stress) ↓ (53%) • Fibrinogen (marker of blood coagulation) ↔	• IL-8 (systemic inflammation) ↓ (58%)[d] • Exhaled breath condensate measures ↔ • Lung function measures ↔ • Blood pressure ↔ • Heart rate variability ↔	Airway impedance ↓ (7%) Airway resistance ↓ (7%) Small airway resistance ↓ (20%) Von Willebrand factor (vWF) ↓ (27%) FEV1 and FVC ↔ Blood pressure ↔ IL-6 ↔
Assessment of study strength	Strong (randomized, blind, crossover intervention with large sample size and long sample duration)[c]	Moderate (randomized, blind, crossover intervention), but short duration and small sample size	Strong (randomized, blind, crossover intervention with medium/large sample size but short duration)
Author(s) main conclusion(s)	"...air pollution exposure was associated with systemic inflammation, oxidative stress and elevated blood pressure." And "the long-term filtration of air pollution with an air conditioner filter was associated with cardiovascular health of adults."	"...results showed that indoor air filtration produced clear improvement on indoor air quality, but no demonstrable changes in the cardio-respiratory outcomes of study interest observed in the seniors living with real-world air pollution exposures."	"A single overnight residential air filtration, capable of reducing indoor particle concentrations substantially, can lead to improved airway mechanics and reduced thrombosis risk."

Not in Fisk (2013)

The only long-term study

Summary of non-allergies/asthma intervention studies

- 11 intervention studies investigated air cleaner use and primarily cardiovascular health outcomes or markers of these health outcomes in subjects without allergies and asthma
  - 4 from Fisk (2013) and 7 new studies (10 short-term, 1 long-term)
    - 8 investigated portable air cleaners (mostly HEPA)
    - 2 investigated central in-duct or window mounted PM filters
    - 1 investigated a window unit with outdoor air supply + filter
- 10 of the 11 studies reported statistically significant improvements in at least one measured outcome
  - Lung function, exhaled breath condensate, blood pressure, and/or heart rate, while markers of health outcomes include biomarkers of microvascular endothelial function, inflammation, oxidative stress, and/or lung damage
- Magnitudes of improvements typically 5-10%
  - One long term study showed greater improvements

Summary of air cleaner health intervention studies

Of the 19 residential intervention studies reviewed:

- 18 studies found statistically significant reductions in indoor concentrations of $PM_{2.5}$, PM_{10}, and/or particle number counts with the use of air cleaners (mostly portable air cleaners)
- PM ($PM_{2.5}$/PM_{10}/PNC) concentration reductions with HEPA or equiv. portable air cleaners were typically 50% or more
- Only a few studies investigated central in-duct filtration
  - Reductions in indoor PM concentrations not as consistent
  - Low system runtimes?
- Allergens in dust were only sometimes affected in a small number of studies that measured allergens

Summary of air cleaner health intervention studies

Of the 19 residential intervention studies reviewed:

- 18 studies also reported statistically significant associations between the use of air cleaners and at least one measure of health outcomes or marker of health outcomes
- Magnitude of health improvements were relatively modest
- When multiple outcomes were measured, only a few were affected

Overall Summary:

- Findings continue to suggest that air cleaning (primarily particle filtration by portable air cleaners with appropriately sized clean air delivery rates) in homes can reduce indoor PM concentrations of various sources and sizes by an average of approximately ~50%
  - And that some moderate positive health outcomes have been observed in nearly every study

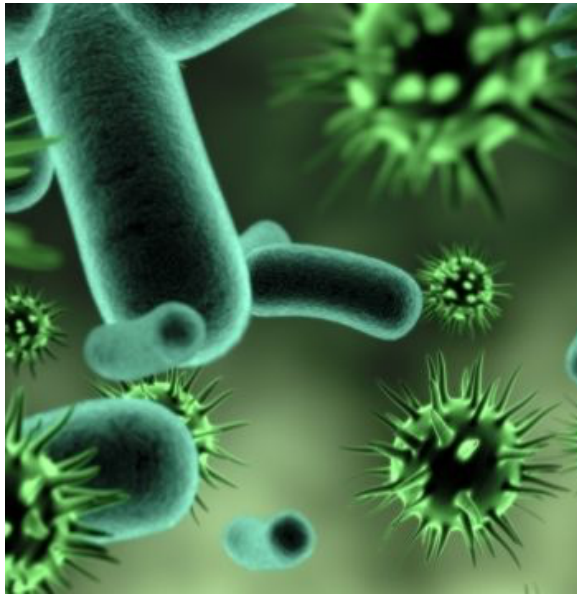
Overall summary of indoor air and health

- We have **a lot** of information about adverse health effects and outdoor air pollution
  - Animal studies, cell level studies, epidemiology studies
- We have **much less** information about indoor air and adverse health effects
  - Most of this information suggests strong connections
- There are new methods/efforts to link epidemiology functions to indoor air pollutants to estimate health effects across the building stock
  - Including under changing conditions (e.g., ventilation, filtration, or source control); still a burgeoning field of study
- There is a need for **more direct** indoor epidemiology studies

INDOOR MICROBIOLOGY

Microbiology of the built environment (MoBE)

- Human health depends in part on the interactions between humans and the microbiology of buildings
  - Microbes can cause adverse health effects
  - Microbes can also provide protective benefits
- The climate, materials, and design of artificial environments and human behavior has consequences for human health
- A deeper understanding of the complexity of indoor microbial communities can help us understand the net impacts of microbes in buildings



Exposure to microbes and human health

Potential for adverse effects

- Microbes can irritate airways
  - Endotoxins (found in outer membrane of microbes)
  - Moisture damage → Toxin release (e.g., microbial VOCs) from mold (fungi)
  - Allergens (e.g., dust mites, cockroach allergens) exacerbate asthma symptoms
- Microbial infections
  - Bacterial, viral, and fungal

Potential for beneficial effects

- Microbial exposure can influence innate immunity and development of the immune system
  - A specific species?
  - A specific microbial structure?
  - Microbial diversity?

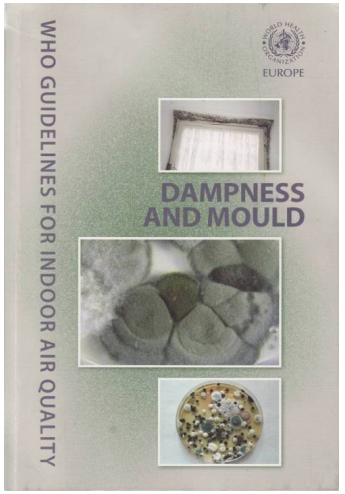
Health effects associated with exposures in damp indoor environments

WHO Dampness & Mold Guidelines 2009, Mendell et al. 2011 *EHP*, and Kanchongkittiphon et al. 2015 *EHP*:

- **Causal** connection with exacerbation of asthma in children and "dampness" in buildings
  - "Do you see or smell mold or water damage?"
- **No causality, but sufficient epidemiological evidence of increased:**
  - Upper respiratory tract symptoms (coughing, wheezing, etc.)
  - Respiratory infections
  - Development of asthma
  - Bronchitis
  - Allergic rhinitis
- Interestingly, no associations between quantifiable microbial measures and respiratory health effects (some suggestive associations)
  - Toxicology studies suggest the associations are real

Do microbes explain the association between dampness and health?

- We don't know (WHO 2009)
- The most likely candidate:
  - Dampness increases microbial growth (particularly fungal/mold)
- But which type of microbes, metabolites, etc.?
  - Not known
  - No dose-response data
  - No possibility to conduct risk assessment, set guidelines, separate between harmless and harmful exposure



Prevalence of building dampness

- WHO (Europe), dampness data from the member countries (2007): on average, 18% of population is exposed to dampness (range 5-37%)
- IOM 2004: 20% of buildings in North America have signs of dampness
- Mudarri and Fisk 2007 *Indoor Air*: prevalence of dampness and mold in houses ~50%

- General weaknesses of such assessments:
  - No standard metrics to measure/quantify dampness
  - Links to health still poorly understood

Economic importance of mold/dampness in buildings

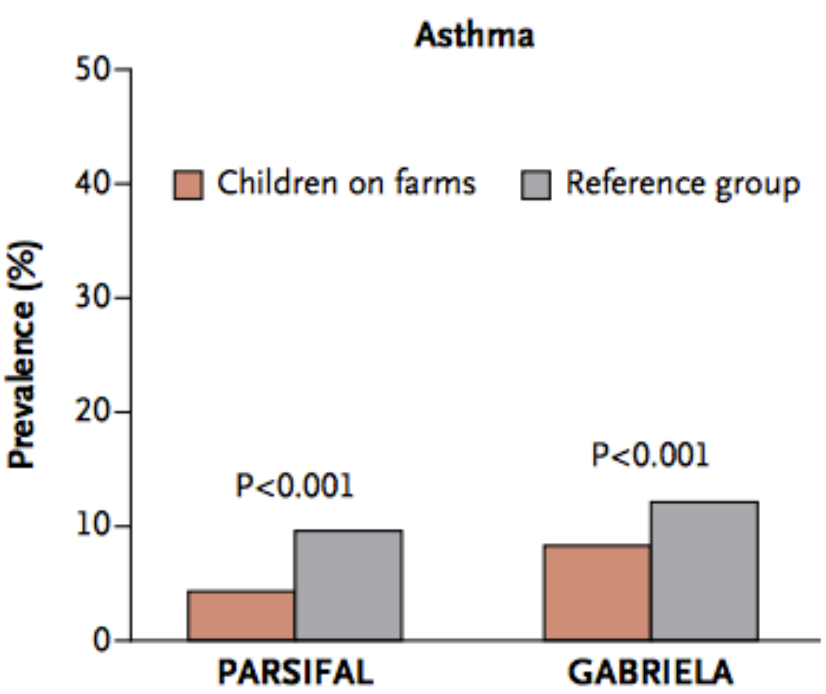
- In the U.S., 21% (95% CI 12-29%) of asthma cases likely attributable to mold/dampness exposure
- 4.6 (2.7-6.3) million cases of asthma attributable to mold/dampness
- Annual cost of mold-related asthma: $3.5 billion USD
- Conclusion: Exposure to dampness and mold in buildings poses a significant public health and economic risk in the US

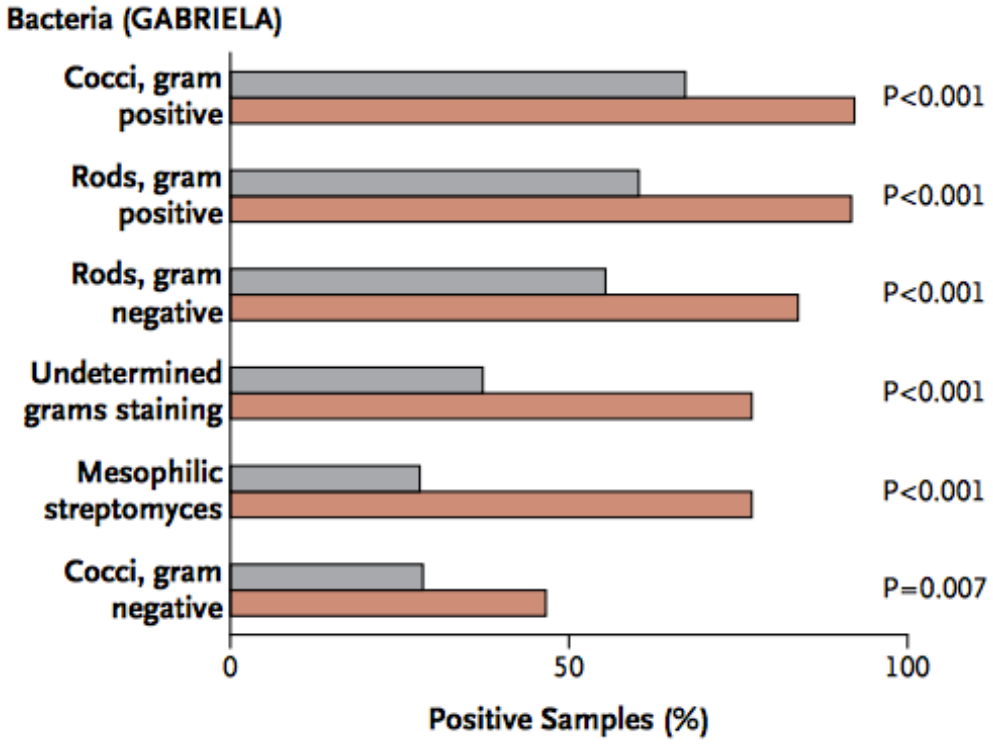
Mudarri and Fisk **2007** *Indoor Air* 17:226–235

The ‘hygiene-hypothesis’

... children that are exposed to high levels of biological agents at early age in life, predominantly in the countryside, are less prone to become allergic than children that grow up in urban environments ...

Microbial diversity and asthma





Ege et al. **2011** *NEJM*

Microbial diversity and asthma

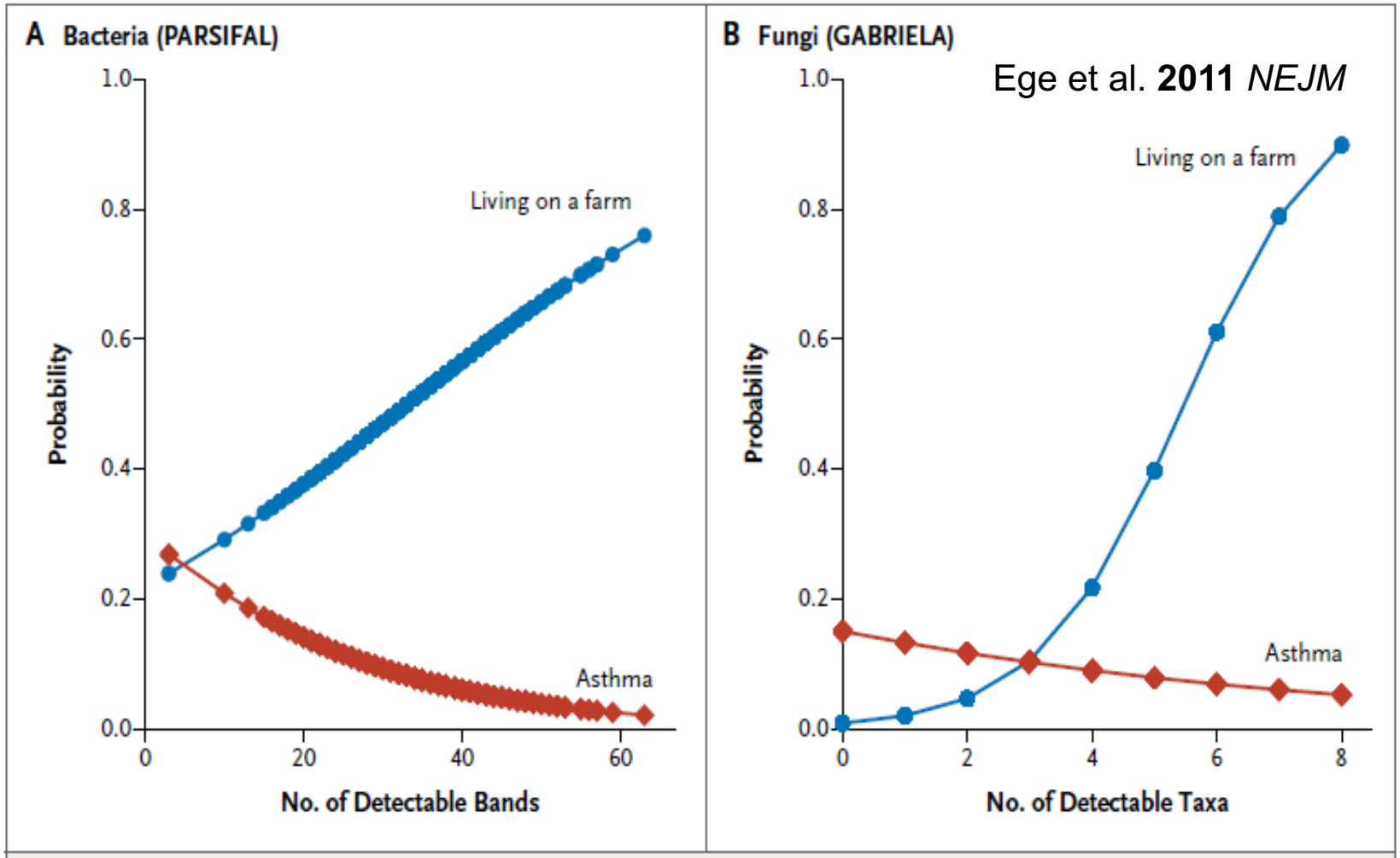


Figure 3. Relationship between Microbial Exposure and the Probability of Asthma.

In both the PARSIFAL study and GABRIELA, the range of microbial exposure was inversely associated with the probability of asthma.

Indoor microbes and health

- Environments rich in microbes are associated with:
  - Protection from asthma (farms, pets)
  - Increased risk of asthma (moisture damage)

- What makes microbial exposure beneficial or harmful?
  - For potential pathogens, what is the infectious dose and where does the pathogen enter the body?
  - For potentially protective exposures, is it microbial diversity? Quantity? Certain taxa? Metabolites? Or Timing?

- Challenges
  - Better measures of exposure to microbes
  - Better epidemiological studies

HOW DO WE ASSESS MICROBES IN BUILDINGS?

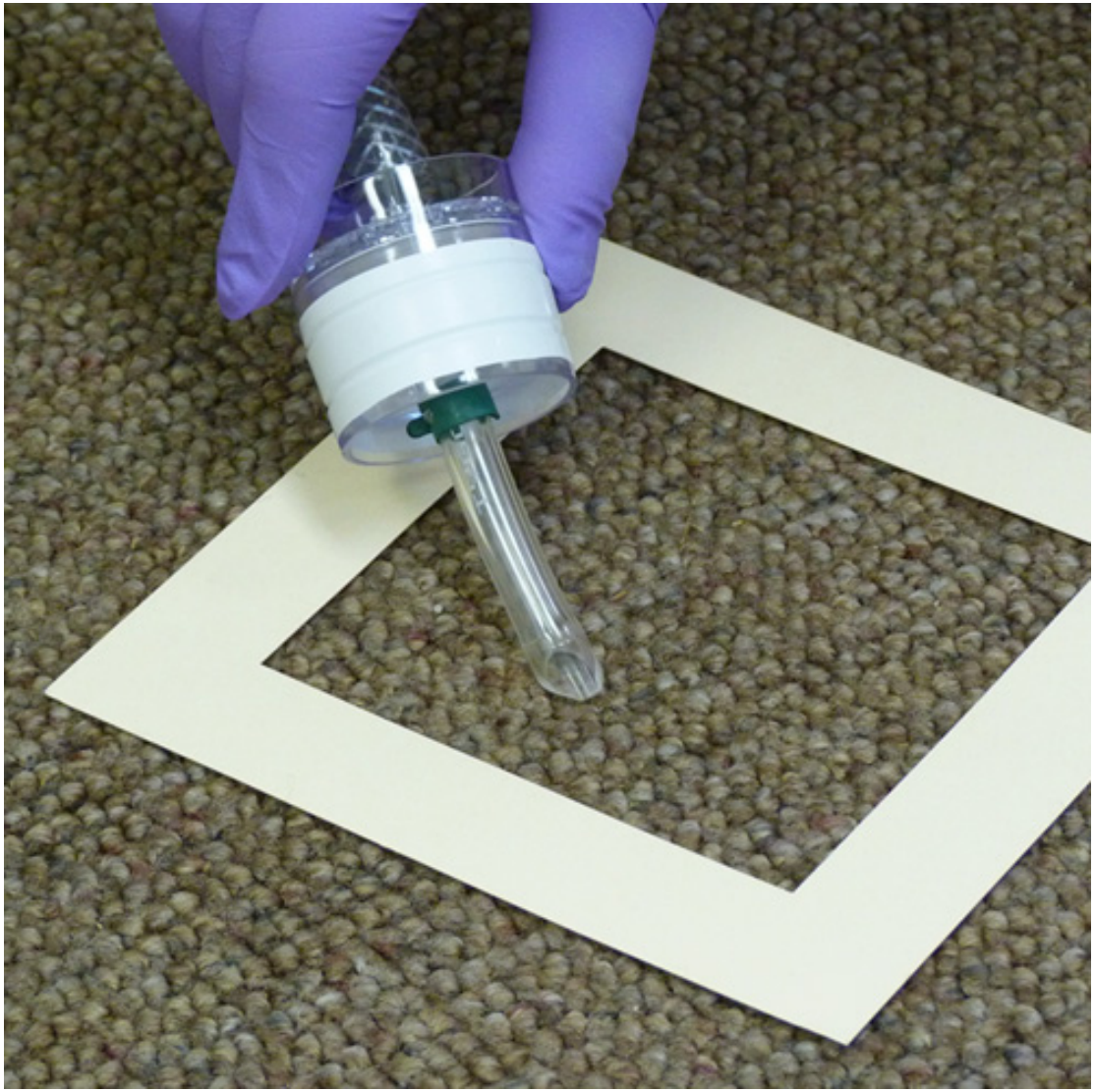
How do we study indoor microbes?

- Environmental sample collection (collect biomass)
  - Air
  - Surfaces
  - Building materials
  - Water

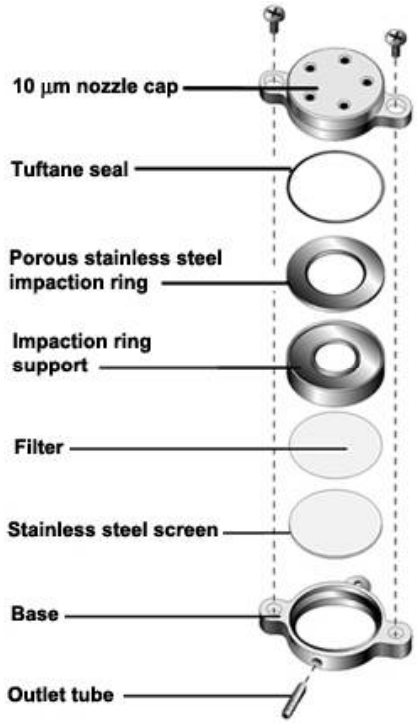
- Sample analysis (analyze biomass)
  - Culture-based methods
  - Culture-independent methods
    - Biomass surrogates (cell wall markers)
    - DNA based methods (qPCR, NGS)

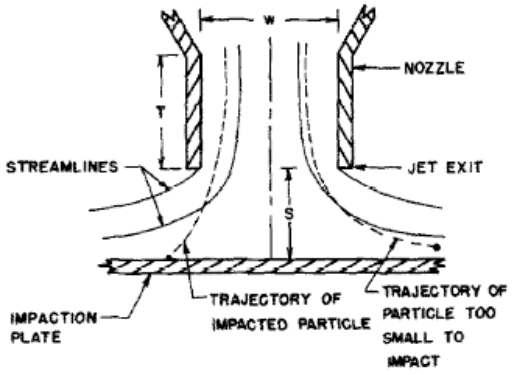
Surface sampling

House dust collection



Air sampling





Impactors

Liquid impingers

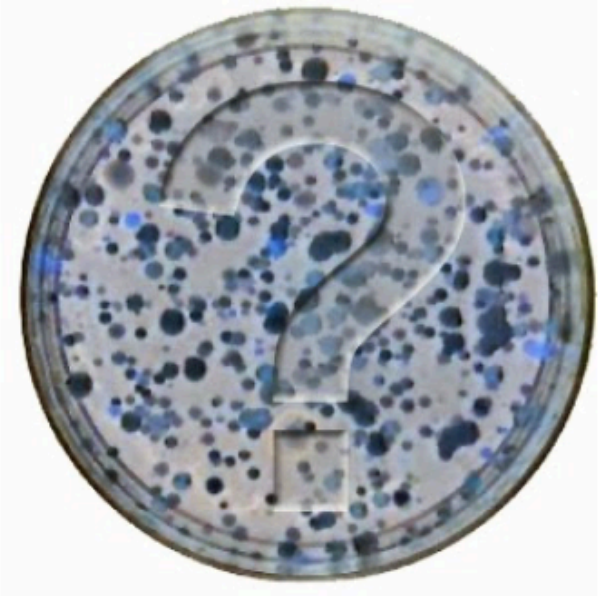
Size-fractionated sampers

Culture-based techniques

- Culture growth
  - Solid media
  - Liquid media
  - Different types of microbes form colonies with different characteristics
- Microscopy and staining techniques
  - Identify physical characteristics (rod, sphere, helix)
- Unfortunately, many microbes look similar to one another and many do not grow outside of their natural habitats

Why not use culture-based methods?

- The great plate count anomaly



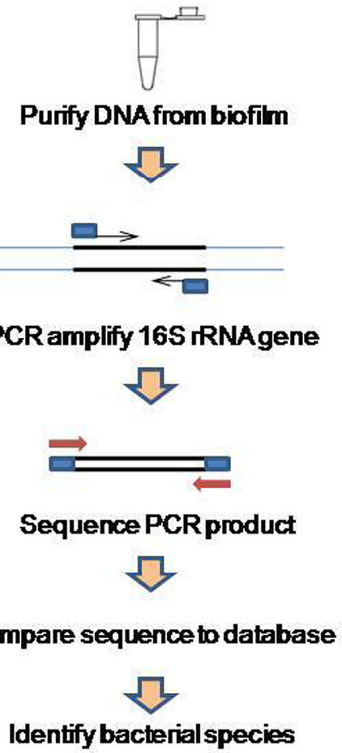
Habitat	Culturability (%)
Seawater	0.001-0.1
Freshwater	0.25
Mesotrophic lake	0.1-1
Estuarine waters	0.1-3
Activated sludge	1-15
Sediments	0.25
Soil	0.3
Air	~1

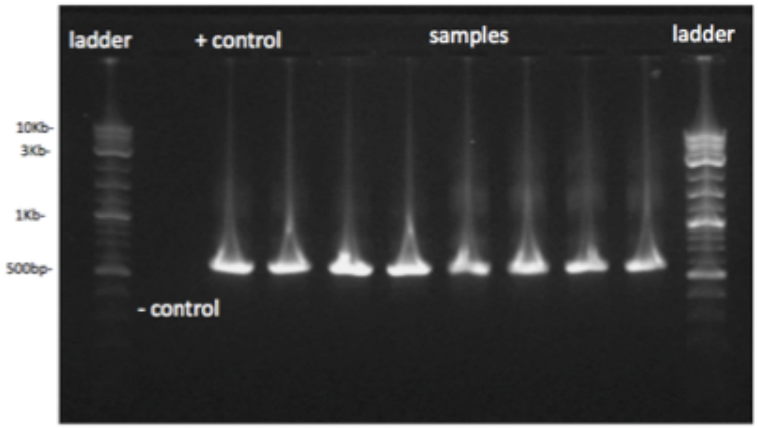
Culture-independent methods

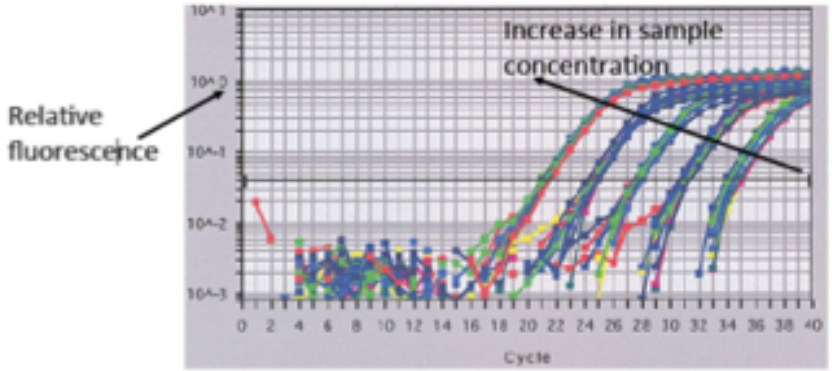
- Polymerase chain reaction (PCR) amplification
  - qPCR
- Sequencing of genes encoding small subunit ribosomal RNA (e.g., 16S rRNA)
  - 16S rRNA is ~1500 nucleotides long, present in all organisms, evolved slowly and includes conserved and variable regions
- Shotgun metagenomics
- **Process for all:** Collect sample, filter biomass, extract DNA (or RNA), and analyze DNA (or RNA)
  - You end up with a sequence of nucleobases (ATCG)
    - Sample: atgcaagtcgaacgcyctctccgcgaggggagggagtggcggacgggtgaggaacacgt gggtgacctgccctgcagtgggggataccg

Culture-independent methods: PCR

- Polymerase chain reaction (PCR) amplification (and Quantitative PCR, or qPCR)
  - Selects gene or segment of DNA from the total DNA extracted (using primers)
    - Primers are small single stranded DNA complementary to the sequence flanking the target sequence or gene of interest
  - Then copies of the DNA (amplicons) are made
  - Fluorescent dyes or probes are added to quantify gene copy number (relative gene expression)





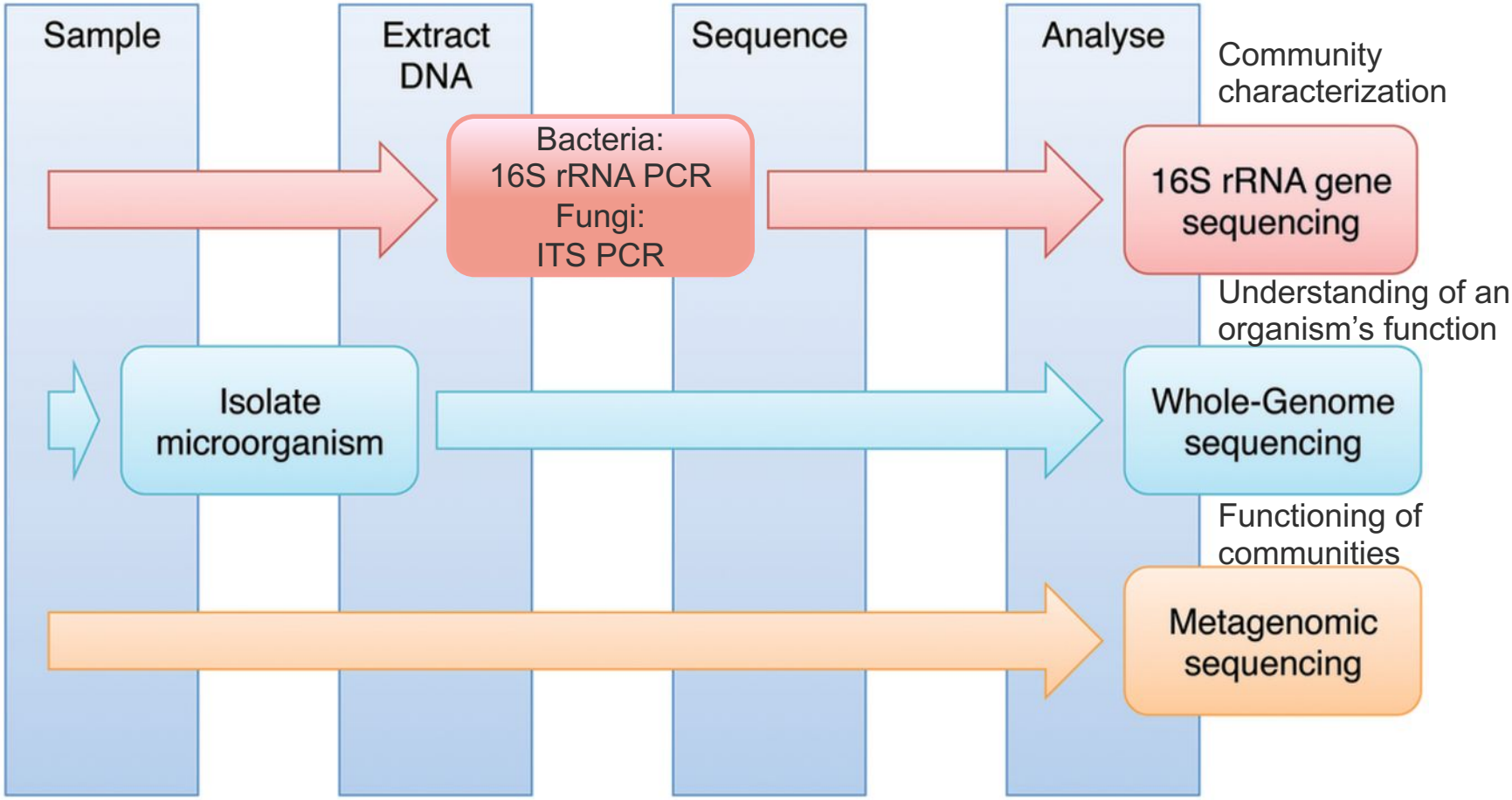


Next generation sequencing and the 'microbiome'

- "Next generation sequencing" (NGS)
  - Also known as "high-throughput sequencing"

- Technologies/techniques include:
  - Includes a number of different modern sequencing technologies (e.g., Illumina, Roche 454, Ion Torrent, etc.)
  - Different techniques (amplicon, genomic, metagenomic, metatranscriptomic, meta-whatever sequencing)
  - Massive parallel sequencing of samples is possible
  - Quick, inexpensive, and produces a massive amount of data

Next-generation sequencing

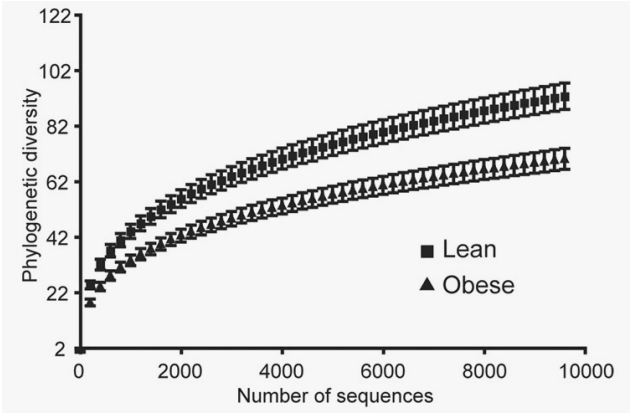


Cox et al. **2013** *Hum. Mol. Genet.*

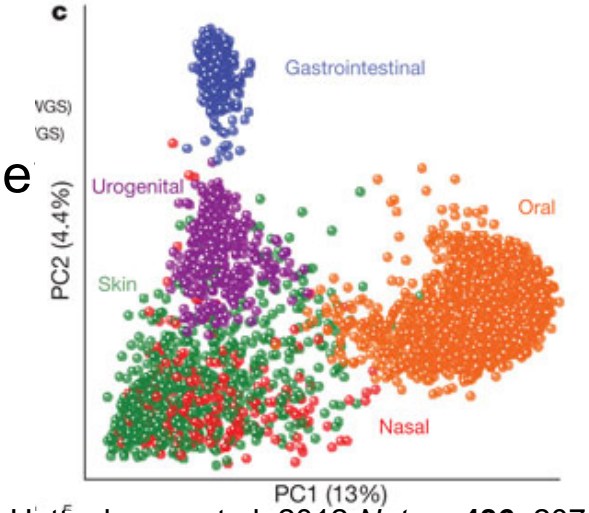
Human Molecular Genetics

What can culture-independent methods tell you?

- PCR: How many gene copies are there?
  - Specific target (specific bacterium or virus)
- Taxonomy
  - Who's there? What groups do they belong to?
  - Number of operational taxonomic unit (OTUs) based on DNA sequence data
- Alpha diversity
  - Within sample diversity (e.g. richness, Shannon Index)
  - How many OTUs (or taxa) are in my sample
- Beta diversity
  - Between sample diversity and relatedness
  - Does my sample 'look like' others?



Turnbaugh et al. 2009 *Nature* 457: 480-484



Huttenhower et al. 2012 *Nature* **486**, 207-214

What don't culture-independent methods tell you?

- Culture-independent (molecular) methods don't tell you whether or not the organism that the DNA (or RNA) comes from is **viable**

- It only verifies that the particular organism was present at some point in time, but may no longer be viable

- Many molecular methods also only provide relative abundance and not absolute abundance

- Viability is especially important for verifying pathogen potential
  - And requires a different suite of tools

WE'VE BEEN STUDYING INDOOR MICROBES FOR A LONG TIME…

Leprous plague in the house

(From the Bible)

- The initial responsibilities of the owner and priest are given in *Leviticus 14:33-38*

- Instructions of what to do after the quarantine of seven days is complete: *Leviticus 14:39-42*

- Instructions for what happens if leprosy returns to a house after it has been treated: *Leviticus 14:43-47*

Laws for Cleansing Houses, Leviticus ch. 14, 33-53, The Old Testament

... then he who owns the house shall come and tell the priest, 'There seems to me to be some case of disease in my house.' Then the priest shall command that they empty the house before the priest goes to examine the disease, lest all that is in the house be declared unclean. And afterward the priest shall go in to see the house. And he shall examine the disease. And **if the disease is in the walls of the house with greenish or reddish spots**, and if it appears to be deeper than the surface, then the priest shall go out of the house to the door of the house and **shut up the house seven days**. And the priest shall come again on the seventh day, and look. **If the disease has spread in the walls of the house, then the priest shall command that they take out the stones in which is the disease** and throw them into an unclean place outside the city. And **he shall have the inside of the house scraped all around**, and the plaster that they scrape off they shall pour out in an unclean place outside the city. Then they shall take other stones and put them in the place of those stones, and he shall take other plaster and plaster the house.
"**If the disease breaks out again in the house**, after he has taken out the stones and scraped the house and plastered it, then the priest shall go and look. **And if the disease has spread in the house, it is a persistent leprous disease in the house; it is unclean. And he shall break down the house,** its stones and timber and all the plaster of the house, and he shall carry them out of the city to an unclean place. Moreover, whoever enters the house while it is shut up shall be unclean until the evening, and whoever sleeps in the house shall wash his clothes, and whoever eats in the house shall wash his clothes. ...

Carnelley et al. (1887)

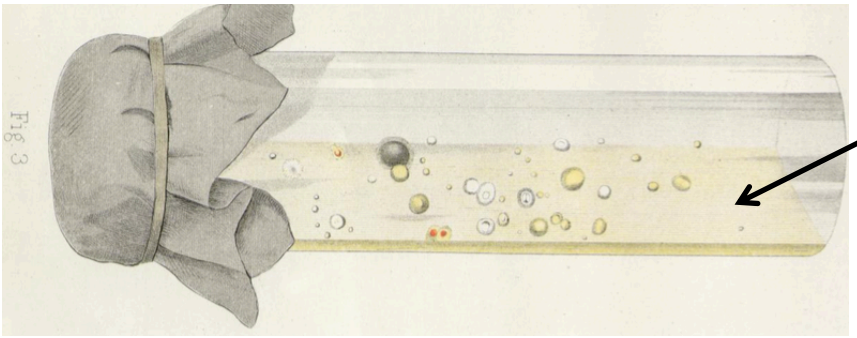
IV. *The Carbonic Acid, Organic Matter, and Micro-organisms in Air, more especially of Dwellings and Schools.*

By Professor Thos. Carnelley, *D.Sc., and* J. S. Haldane, *M.A., M.B., University College; and* A. M. Anderson, *M.D., Medical Officer of Health, Dundee.*

Communicated by Sir Henry E. Roscoe, *F.R.S.*

Received June 10,—Read June 10, 1886.

5. An investigation into the sources of the organic matter and micro-organisms of air inside buildings, and the circumstances affecting the number of micro-organisms; also of the relative number of bacteria and moulds in both outside and inside air.



Carnelley et al. **1887** *Phil Trans Royal Soc B*

Carnelley et al. (1887)

Always compare indoor air to outdoor air

In order to draw conclusions from an examination of air inside buildings, it is of course necessary to know the state of the outside air. As regards each of the constituents estimated, considerable variations were found at different times and places.

Occupant density drives bacterial counts (but has no impact on fungi)

Cubic space per person.	No. of houses.	Temperature.	Carbonic Acid.	Organic matter.	Total micro-organisms.	Bacteria.	Moulds.
Cubic feet.							
100– 180	14	55	11·5	15·1	80	78	1·8
180– 260	18	54	10·7	15·1	49	47	1·5
260– 340	6	53	10·3	11·8	32	31	0·7
340– 500	4	57	9·2	8·4	42	40	2·1
500–1000	6	54	8·6	5·6	6	6	0
1000–2500	8	53	6·7	3·9	9·1	8·5	0·7
2500–4000	4	57	7·9	5·0	13·1	12·8	0·4

The explanation of the ratio $\frac{\text{Bacteria}}{\text{Moulds}}$ increasing with the vitiation of the air is that moulds come mostly from the outside air. When the air in a room becomes vitiated the bacteria increase largely, while the number of moulds is affected to a relatively much less extent, if at all.

Carnelley et al. **1887** *Phil Trans Royal Soc B*

Carnelley et al. (1887)

Resuspension is a key source of indoor microbes

It has been shown by HESSE (*loc. cit.*) that when a room is left quiet the micro-organisms settle out in a few hours, so that the air becomes comparatively free (cf. TYNDALL'S experiments on sterilisation of air by subsidence). Hence it is clear that a certain amount of physical disturbance in a room is a condition necessary to the presence of micro-organisms in the air. It might naturally be supposed that the effects of physical disturbance would tend to obscure all other factors affecting the number of micro-organisms present in air. It is, therefore, necessary to consider first what, other things being equal, are the limits of the influence of ordinary physical disturbances on the number of micro-organisms.

be expected that a large number of bacteria would be given off from bed clothes when shaken.*

2. The skin and clothes of the persons present in a room at the time of an observation also occur naturally as a probable source of infection of air. That this source, however, is of much less importance than might be supposed may, we think, be shown from our observations.

Carnelley et al. **1887** *Phil Trans Royal Soc B*

Carnelley et al. (1887)

The "pig pen effect" is very real

B. *Cleanliness of rooms and persons* habitually *present in them.*—In order to show the influence of differences as regards cleanliness, we have classified the houses and schools as shown in the following Table. This Table requires no comment. It shows most conclusively the enormous influence of differences as regards cleanliness on the number of micro-organisms.

		No. of cases.	Average space per person.	Average carbonic acid.	Average organic matter.	Average micro-organisms.
One-roomed houses	Clean	1	295	8·0	13·1	18
	Dirty	7	200	9·9	18·1	41
	Dirtier	13	221	10·7	13·5	49
	Very dirty	6	220	11·0	15·1	93
Two-roomed houses	Very clean	2	273	12·2	10·8	10
	Clean	4	264	9·3	7·7	22
	Dirty	7	233	9·4	11·2	69

Carnelley et al. **1887** *Phil Trans Royal Soc B*

Carnelley et al. (1887)

Source (and rate) of ventilation air delivery impacts indoor microbes

	Mechanically ventilated.	Naturally ventilated.
Cubic space per person	1	1·0
Temperature in excess of outside air .	1	0·66
Carbonic acid ,, ,, .	1	1·7
Organic matter ,, ,, .	1	7·0
Micro-organisms ,, ,, .	1	9·2
Bacteria ,, ,, .	1	9·4
Moulds ,, ,, .	1	2·0

**Note: Naturally ventilated spaces had lower ventilation rates than mechanically ventilated spaces*

The all-important argument for mechanical ventilation is that it maintains a certain standard of purity, and, unless some simpler method which will maintain a similar standard can be devised, its adoption in crowded schools seems to be very much required.

Carnelley et al. **1887** *Phil Trans Royal Soc B*

Carnelley et al. (1887)

Indoor microbes and built environment factors are weakly correlated

No constant relation between the quantities of carbonic acid, organic matter, and micro-organisms can be detected in individual cases (see PARKES, p. 147; also DE CHAUMONT, 'Roy. Soc. Proc.,' vol. 23, p. 188). Sometimes we find a high organic matter accompanied by a low carbonic acid, whilst under other circumstances the reverse may be the case. A determination of carbonic acid alone is therefore never a sufficient indication of the purity or otherwise of a given sample of air. Nevertheless, by taking the average of a considerable number of observations, we find that there is a *general* relationship, so that a high carbonic acid is, as a rule, accompanied by a high organic matter, and *vice versâ*, though this is by no means always the case. There appears, however, to be no definite connexion between the number of micro-organisms and the amount of carbonic acid (see page 93).

Carnelley et al. **1887** *Phil Trans Royal Soc B*

Early studies on indoor air fungi

Sources, concentrations, determinants

ATMOSPHERIC MOLD SPORES IN AND OUT OF DOORS

MERFYN RICHARDS, M.A., M.SC., PH.D., CARDIFF, WALES

SINCE the early days of studies in allergy to mold spores there has been among allergists considerable doubt concerning the relative importance of the indoor and outdoor air as a source of mold spores which can give rise to respiratory allergy. In several of the earliest published cases of mold allergy the source of the mold was attributed to the patient's home.[1-3] Such

Richards **1954** *J Allergy* 25:429-439

Early studies on indoor air fungi

- Atmospheric mold spores indoors and outdoors
- Outdoor air was the main source of indoor fungi
- In a normal house, indoor molds were similar to outdoors but in lower concentrations
- Concentrations fluctuated seasonally
- In June-October, *Cladosporium* most prevalent indoors; rest of year, *Penicillium*

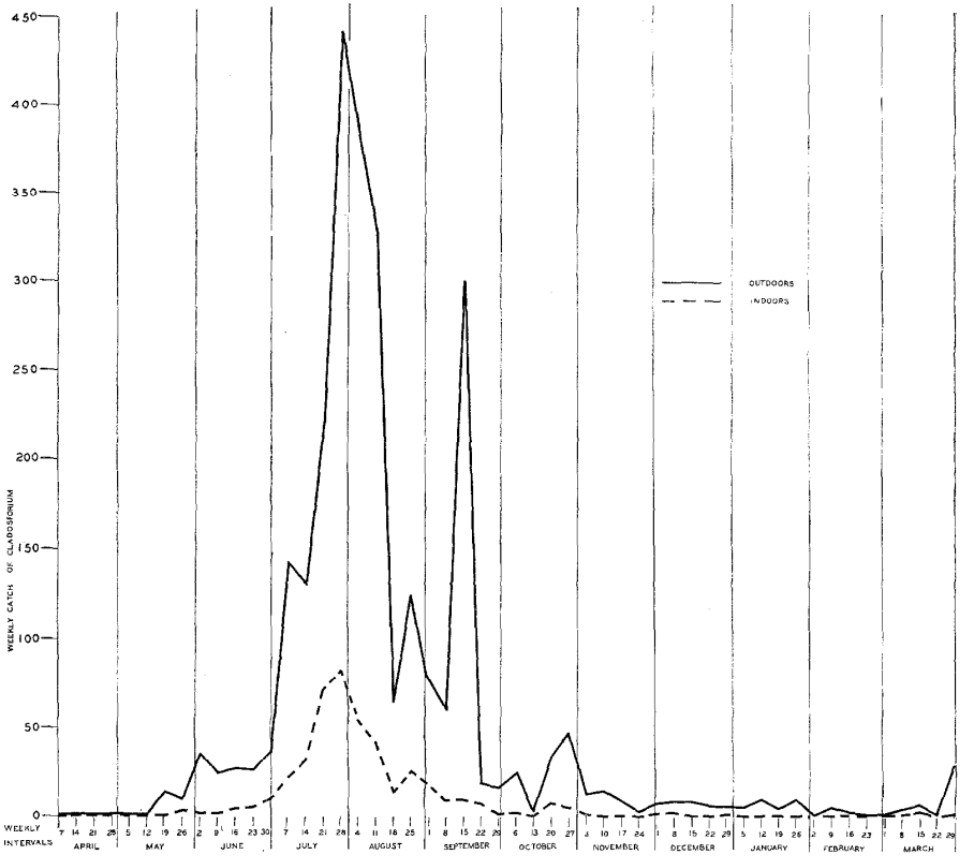


Fig. 3.—The seasonal variation in *Cladosporium* incidence. The graph is plotted at weekly intervals, each point representing the *Cladosporium* catch on six successive daily pairs of plates.

Richards **1954** *J Allergy* 25:429-439

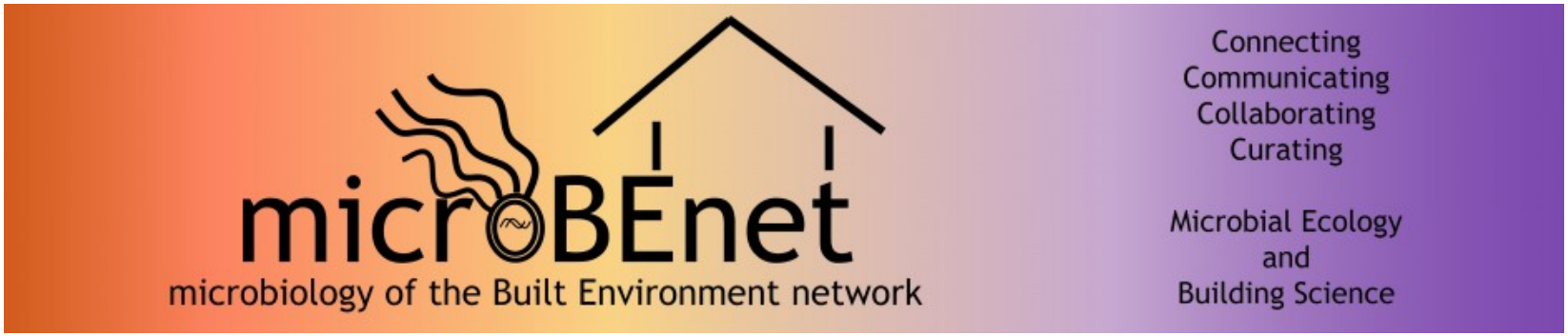
Early studies on indoor air fungi

Richards (1954) also knew the problem of moldy houses:

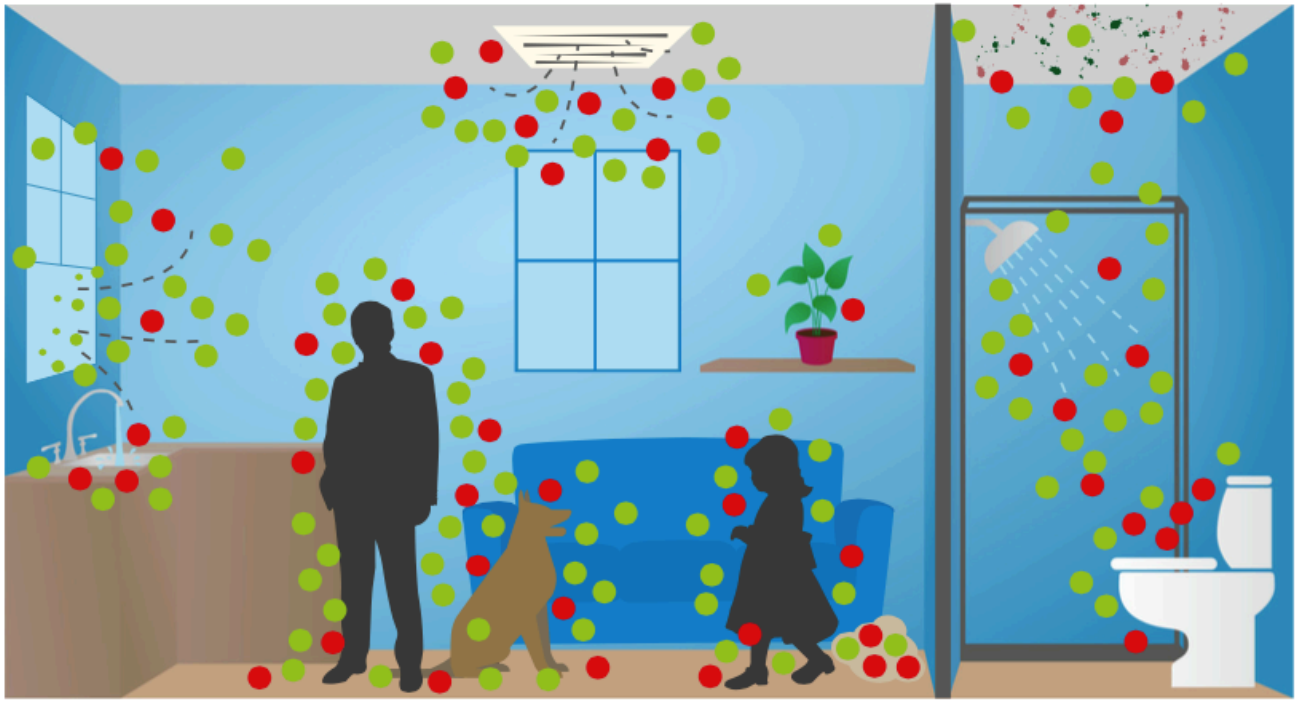
- In (observably) moldy houses, spore content was different in constitution and quantity
- “there can be little doubt that in a house which is visibly moldy the residents are exposed to higher concentrations of mold spores than the residents of a normal, clean, dry house”
- Nilsby (1947): 55 cfu/plate in complaint homes vs. 5 cfu/plate in non-complaint homes

Richards **1954** *J Allergy* 25:429-439

MORE RECENT STUDIES USING CULTURE-INDEPENDENT METHODS



Introduction and motivation



Prussin and Marr **2015** *Microbiome* 3:78

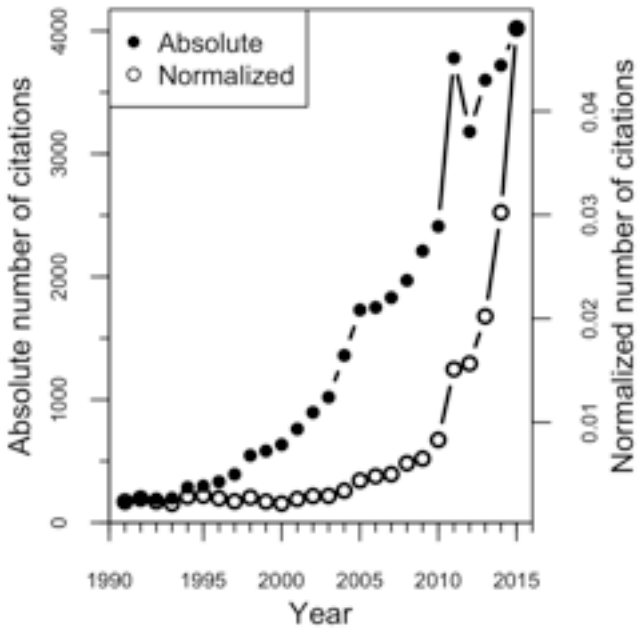
Studying the role of the built environment in exposing humans to specific microbes (e.g., pathogens or allergens) and the role of microbes responsible for the deterioration of building materials has a very rich history

Adams et al. **2016** Ten questions concerning the microbiomes of buildings. *Building and Environment*

Introduction and motivation

There has been a dramatic increase in the use of high-throughput molecular techniques to analyze microbial communities in indoor environments in the last ~10 years

Google Scholar citations by the keywords: *microbiology* OR *microbiome* OR *bioaerosol* AND *indoor*



Adams et al. **2016** Ten Questions concerning the microbiomes of buildings. *Building and Environment*

In a 2016 presentation to the National Academies of Sciences' committee on 'Microbiomes of the Built Environment: From Research to Application', I reviewed recent studies on the microbiology of the built environment (MoBE) and organized their findings into 12 major categories.

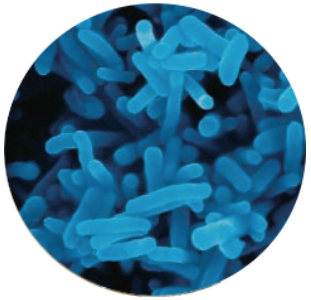
I also proposed that:

1. We have added new layers of complexity to our rich existing knowledge from a long history of applying culture-based methods.
2. The practical implications of this added complexity remain somewhat elusive.

Stephens **2016** *ASM mSystems* 1(4):e00083-16

What have we learned about the built environment microbiome?

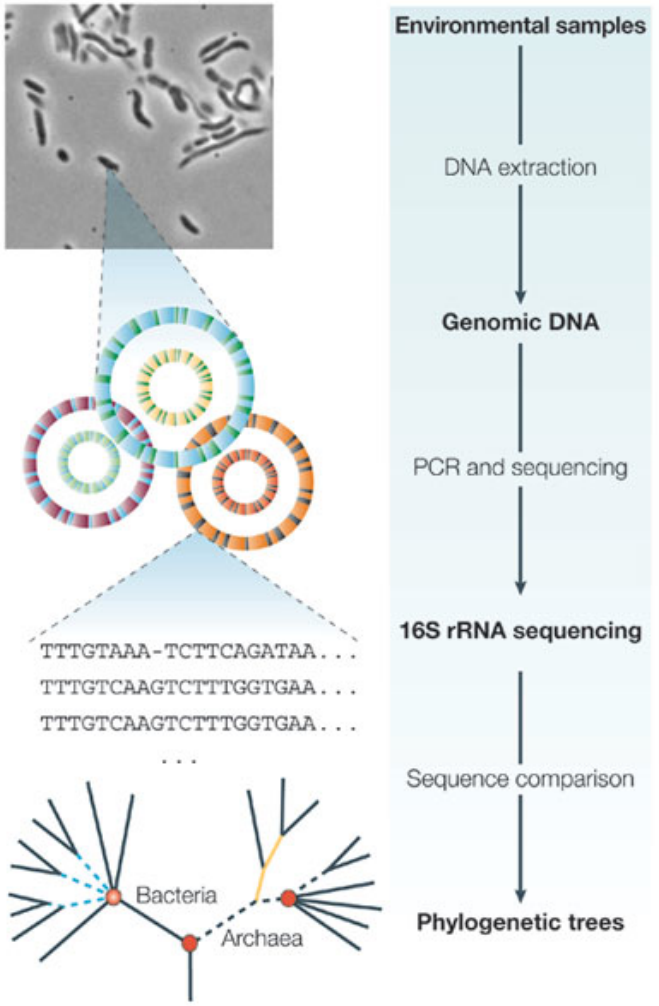
1. Culture-independent methods reveal vastly greater microbial diversity compared to culture-based methods



"The ability to sequence DNA samples from the environment has allowed scientists to detect far more than the 1% of microbes that can be cultured in the laboratory. It has also revealed how they vary from place to place."

Whitfield, J. **2005** *Science* 310:960-961

16S rRNA sequencing



Nature Reviews | Genetics

Tringe, S., Rubin, E. **2005** *Nature Rev Gen* 6:805-814

1. Culture-independent methods reveal vastly greater microbial diversity compared to culture-based methods

Culture-based methods

BASE study (100 offices)

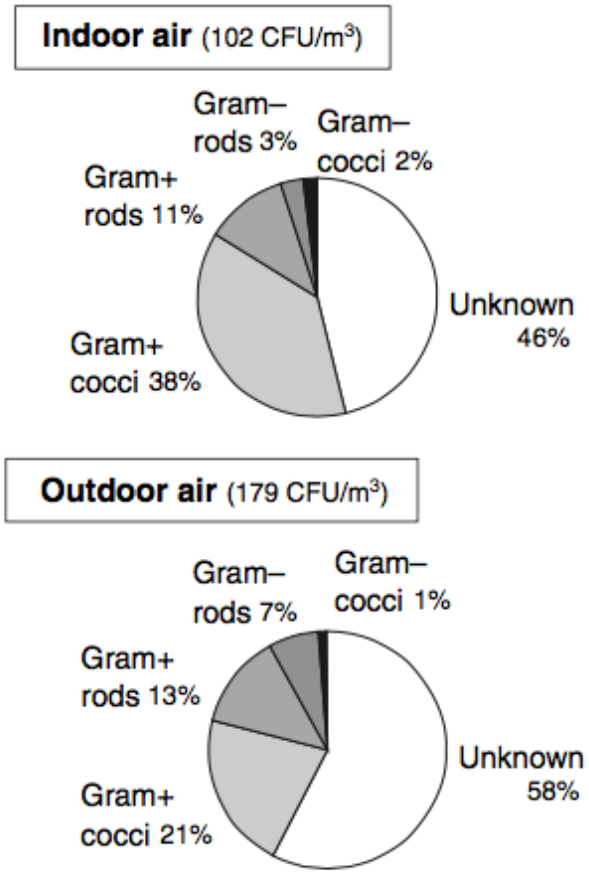
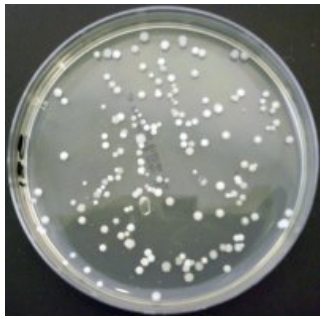
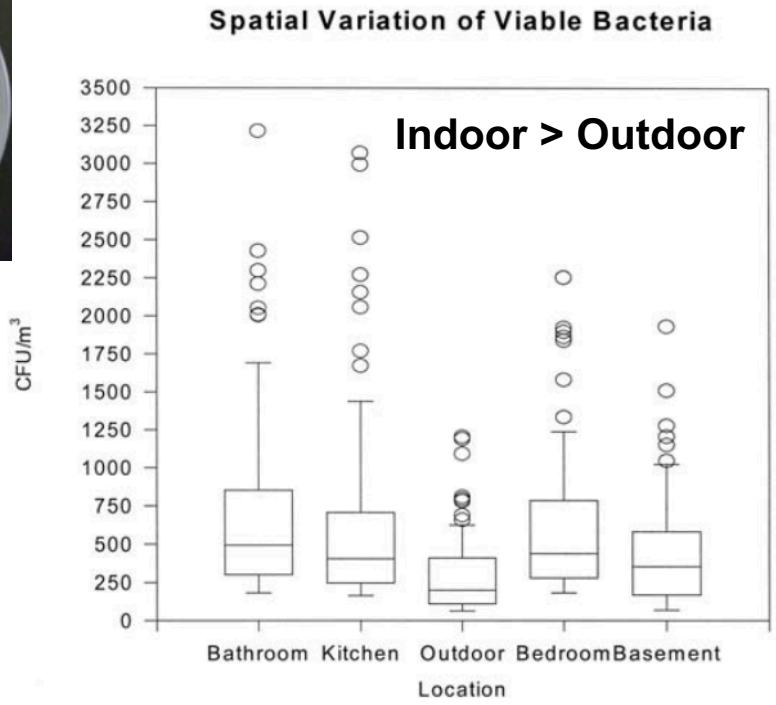


Fig. 1 Composition of culturable bacteria in indoor and outdoor air in 100 large office buildings

Tsai and Macher **2005** *Indoor Air* 15(suppl 9):71-81



Chicago residences (20 homes)

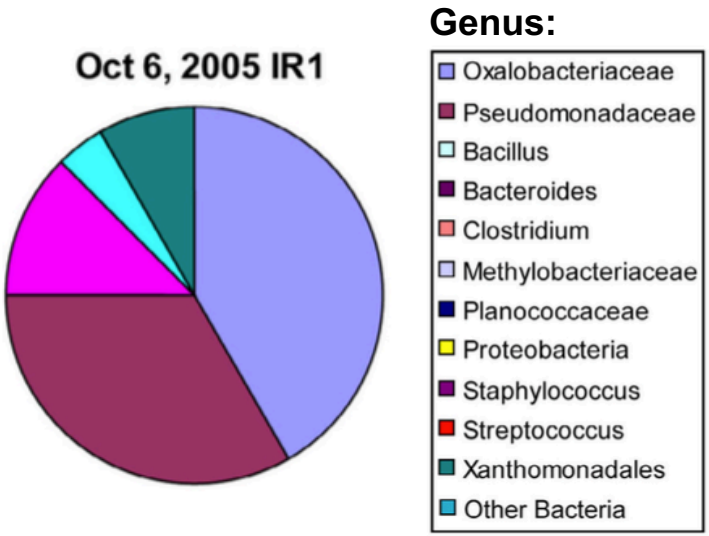


Gram-positive bacteria and *Staphylococcus* sp. levels as a percentage of total culturable bacteria

	Bedroom (%)	Bathroom (%)	Kitchen (%)	Basement (%)	Outdoors (%)
Gram-positive bacteria	58	62	75	68	50
Staphylococcus	37	26	30	16	10

Moschandreas et al **2003** *Aerosol Sci Tech* 37:899-906

1. Culture-independent methods reveal vastly greater microbial diversity compared to culture-based methods

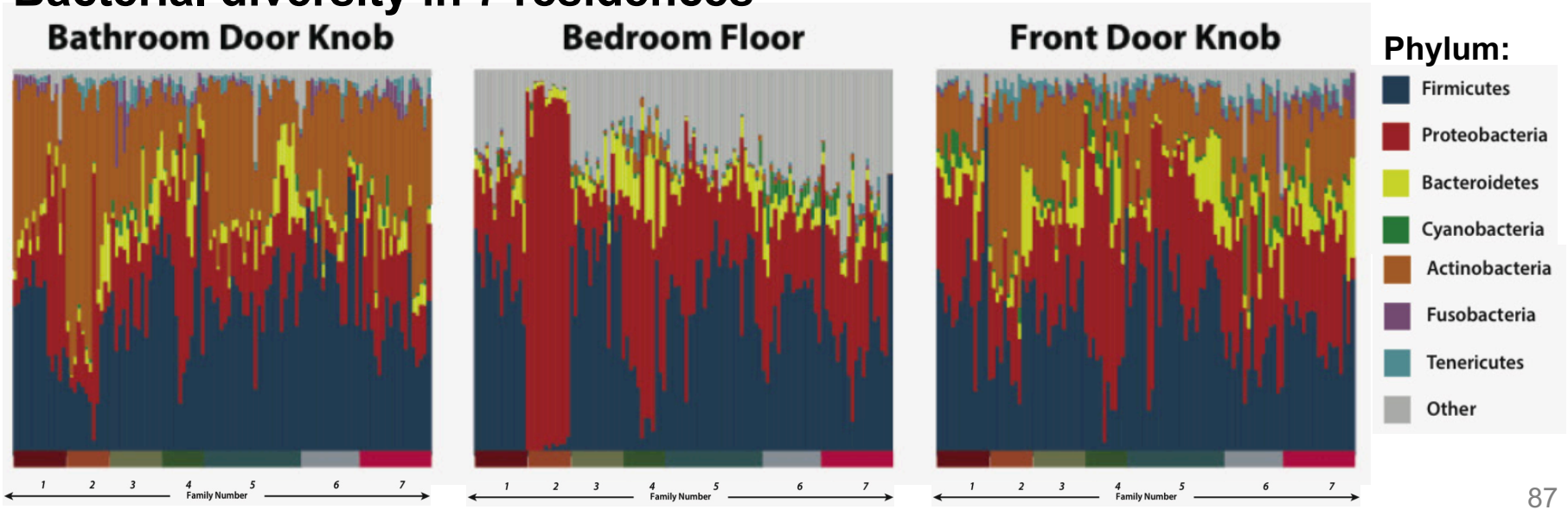


Bacterial diversity in a child-care facility

"Culture-independent methods based on 16S rRNA gene sequencing revealed an entirely new dimension of microbial diversity, including an estimated 190 bacterial species from 15 bacterial divisions"

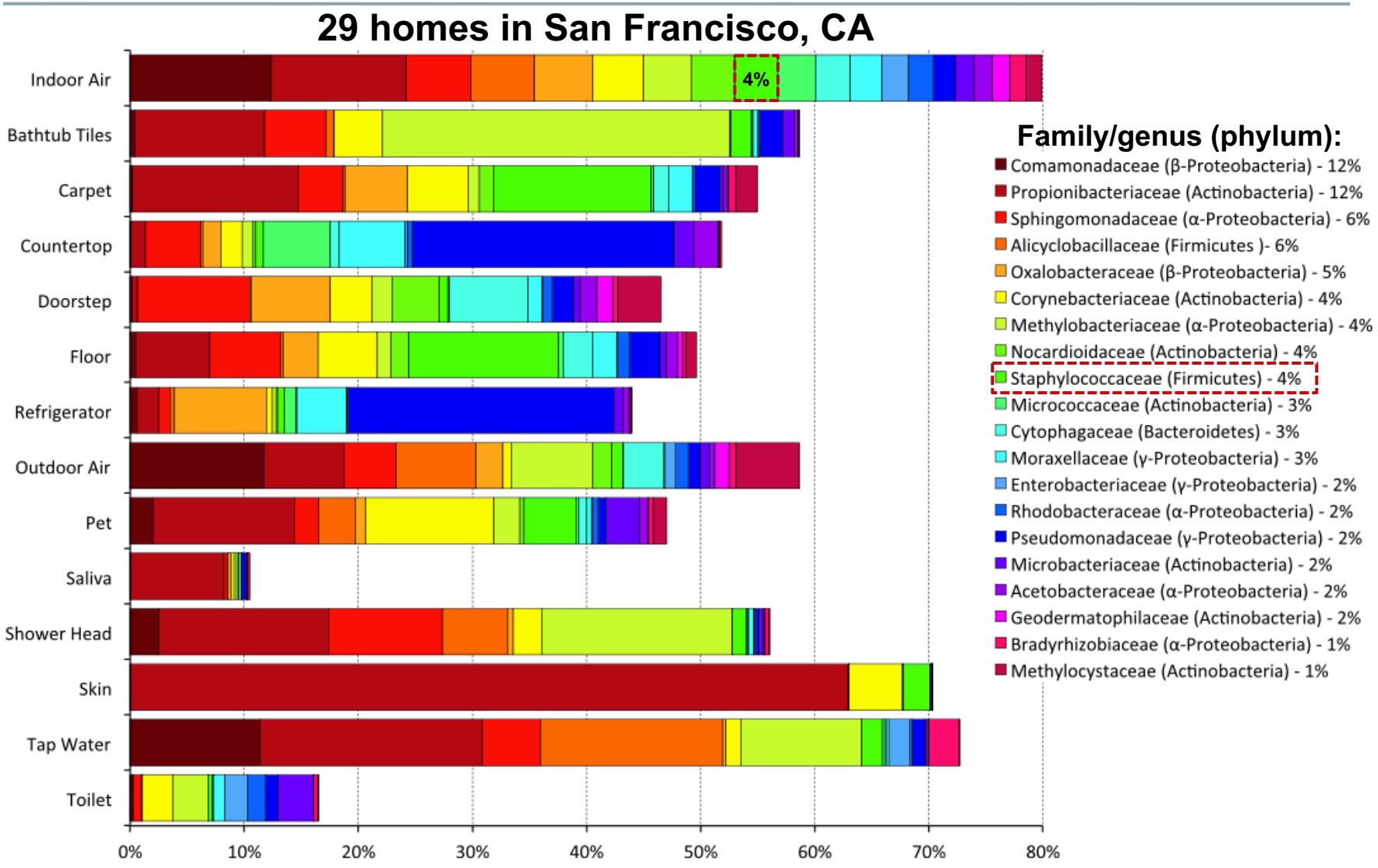
Lee et al. **2007** *BMC Microbiology* 7:27

Bacterial diversity in 7 residences



Lax et al. **2014** *Science* 345(6200):1048-1052

1. Culture-independent methods reveal vastly greater microbial diversity compared to culture-based methods



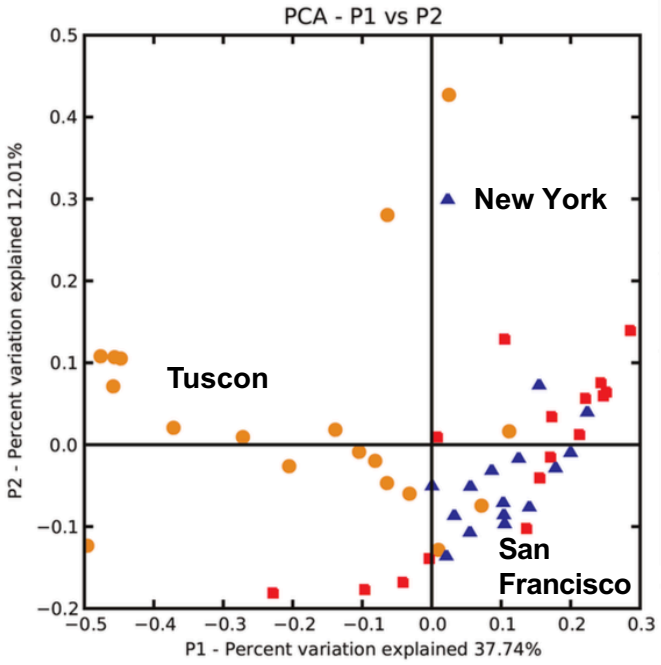
Miletto and Lindow **2015** *Microbiome* 3:61

2. Indoor spaces often harbor unique microbial communities

Bacterial communities on office surfaces in 3 U.S. cities

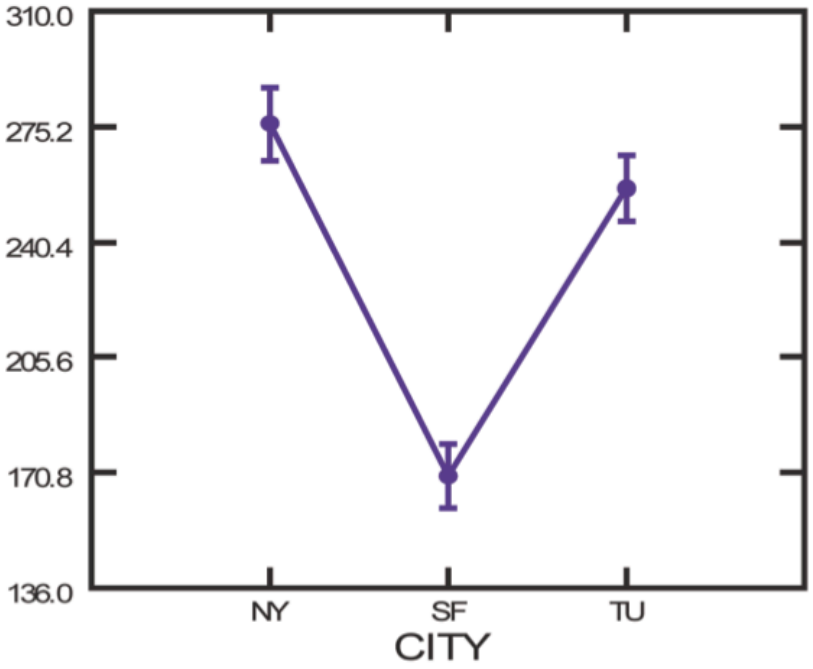
Bacterial diversity

"Bacterial community diversity of the Tucson samples was clearly distinguishable from that of New York and San Francisco, which were indistinguishable"



Bacterial abundance

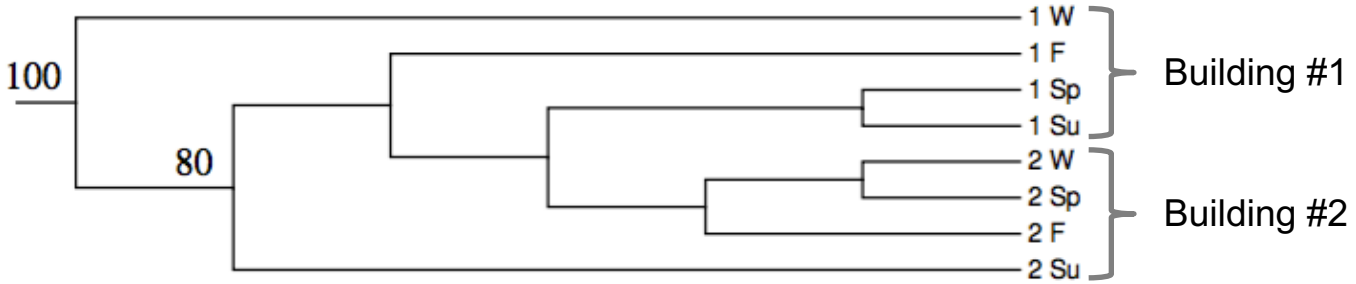
"Multiplex pyrosequencing identified more than 500 bacterial genera from 20 different bacterial divisions. The most abundant of these genera tended to be common inhabitants of human skin, nasal, oral or intestinal cavities."



Hewitt et al. **2012** *PLoS ONE* 7(5):e37849

2. Indoor spaces often harbor unique microbial communities

Offices in two buildings in Finland



Cluster analysis of clone libraries

"The composition and dynamics of indoor dust bacterial flora were investigated in two buildings over a period of one year"

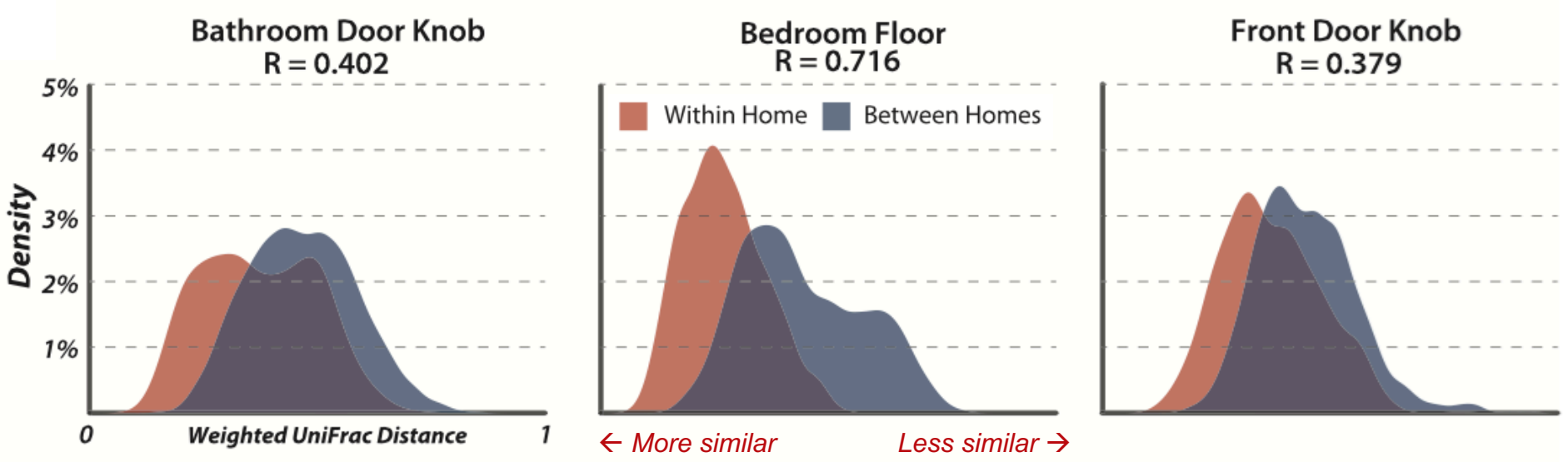
"Bacterial flora of the two buildings differed during all seasons except spring, but differences between seasons within one building were not that clear, indicating that differences between the buildings were greater than the differences between seasons"

"…the bacterial flora of indoor dust is complex and dominated by Gram-positive species. The dominant phylotypes most probably originated from users of the building"

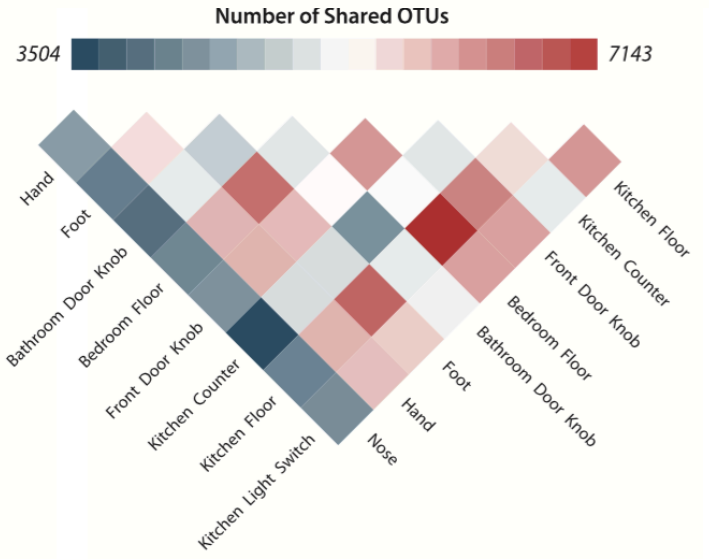
Rintala et al. **2008** *BMC Microbiol* 8:56

2. Indoor spaces often harbor unique microbial communities

7 families and their homes over 6 weeks (including 3 families that moved)



- Microbial communities differed substantially among homes
- Microbiota in each home were identifiable by family
- Floors resemble feet and other floors
- Kitchen counters do not resemble noses



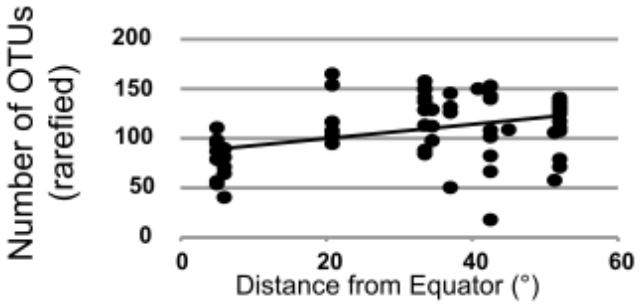
Lax et al. **2014** *Science* 345(6200):1048-1052

3. Indoor fungal communities are largely driven by outdoor fungal communities (in non-damp buildings)

Indoor fungal composition is geographically patterned and more diverse in temperate zones than in the tropics

Anthony S. Amend[a,1], Keith A. Seifert[b], Robert Samson[c], and Thomas D. Bruns[a]

"Contrary to common ecological patterns, we show that fungal diversity is significantly higher in temperate zones than in the tropics, with distance from the equator being the best predictor of phylogenetic community similarity"



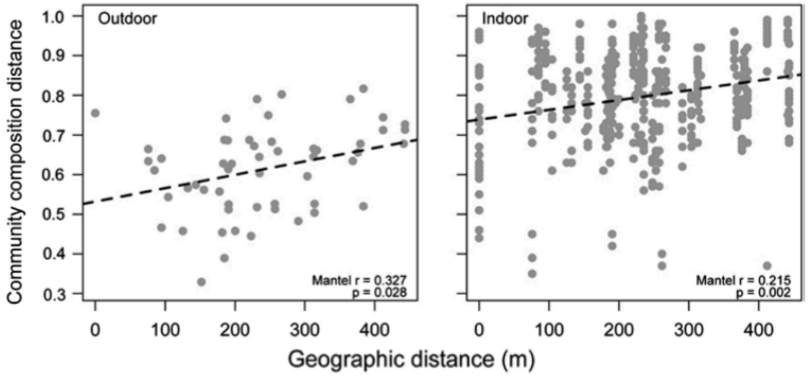
"Remarkably, building function has no significant effect on indoor fungal composition, despite stark contrasts between architecture and materials of some buildings in close proximity"

Amend et al. **2010** *PNAS* 107(31):13748

Dispersal in microbes: fungi in indoor air are dominated by outdoor air and show dispersal limitation at short distances

Rachel I Adams, Marzia Miletto, John W Taylor and Thomas D Bruns
Department of Plant and Microbial Biology, University of California, Berkeley, CA, USA

"Fungal assemblages indoors were diverse and strongly determined by dispersal from outdoors, and no fungal taxa were found as indicators of indoor air"

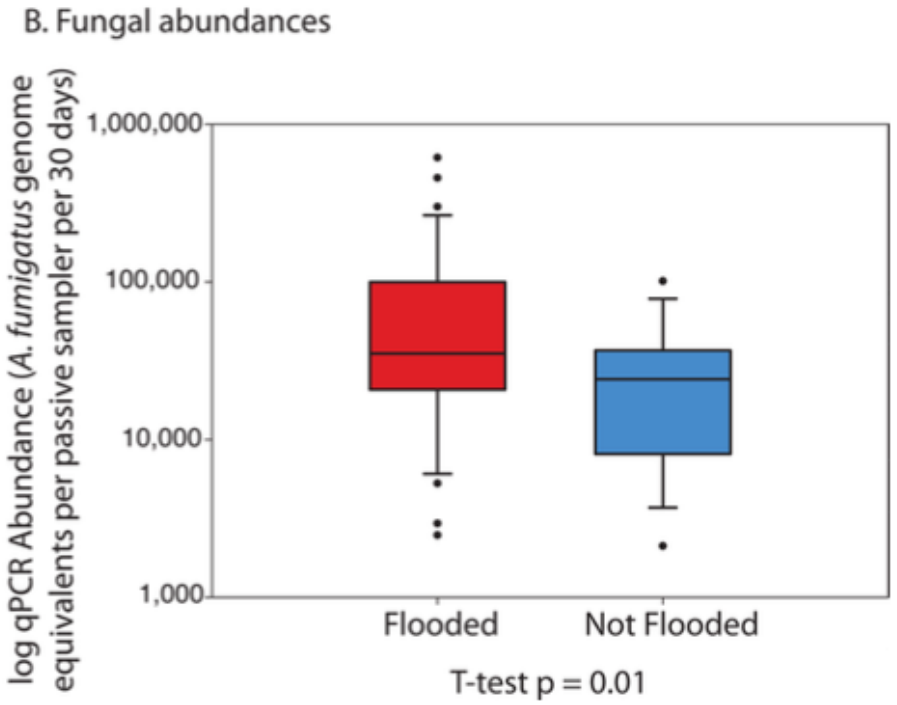


"More fungal biomass was detected outdoors than indoors"
"Room and occupant behavior had no detectable effect on the fungi found in indoor air"

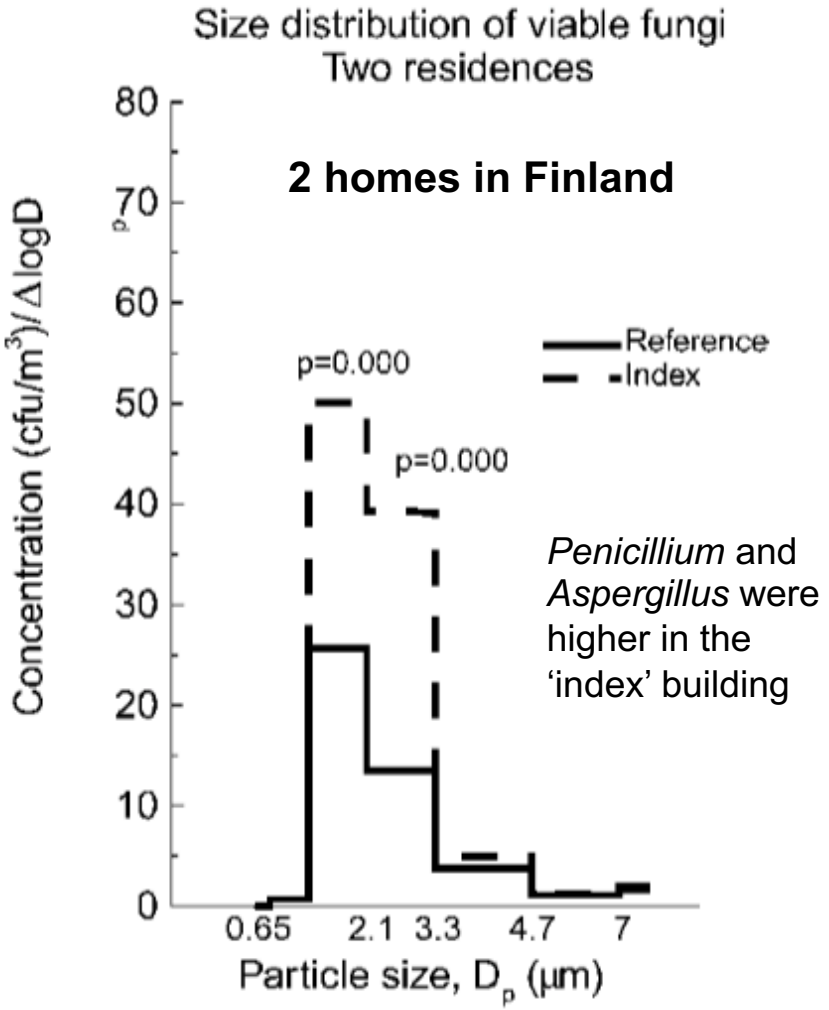
Adams et al. **2013** *ISME J* 1:1-12

4. Indoor fungal communities in damp buildings are often distinct from those in non-damp buildings

36 flood-damaged and 14 non-flooded homes in Boulder, CO



- Fungal abundances were estimated to be 3x higher in flooded homes
- *Penicillium* were the most abundant taxa

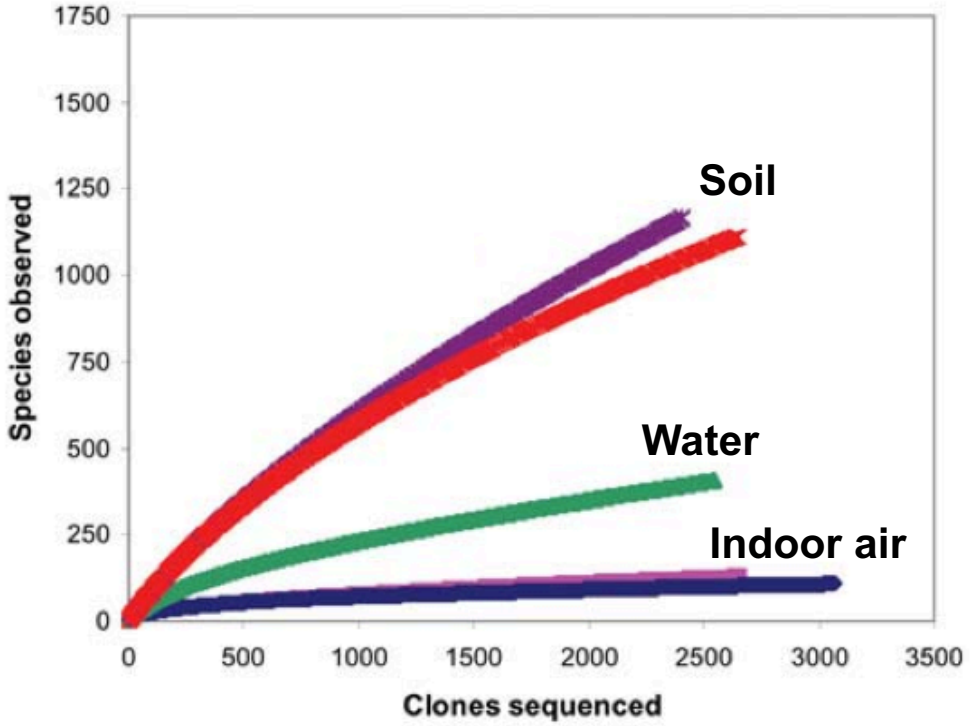


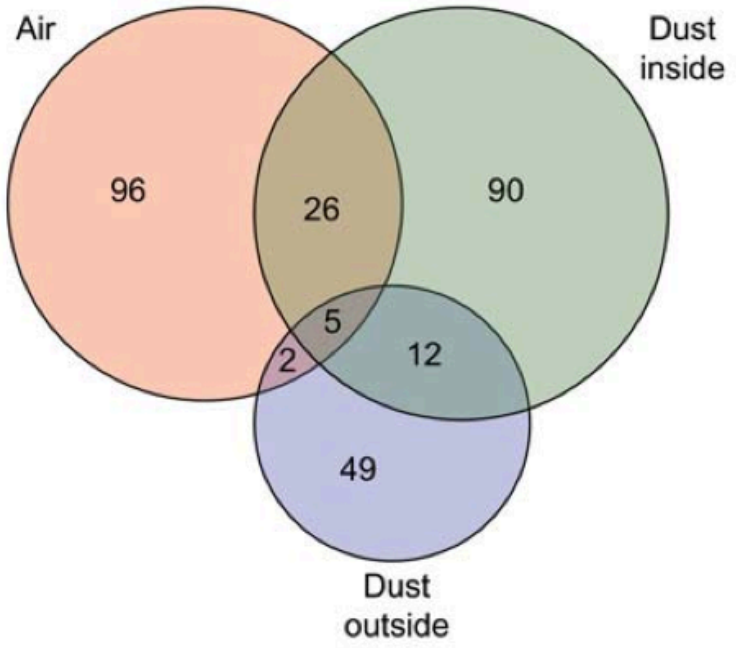
Emerson et al. **2015** *Environ Sci Technol* 49:2675-2684

Hyvärinen et al. **2001** *Aerosol Sci Technol* 35:688-695

5. Indoor bacteria often originate from indoor sources

"Comparison of air samples with each other and nearby environments suggested that the indoor air microbes are not random transients from surrounding outdoor environments, but rather originate from indoor niches."





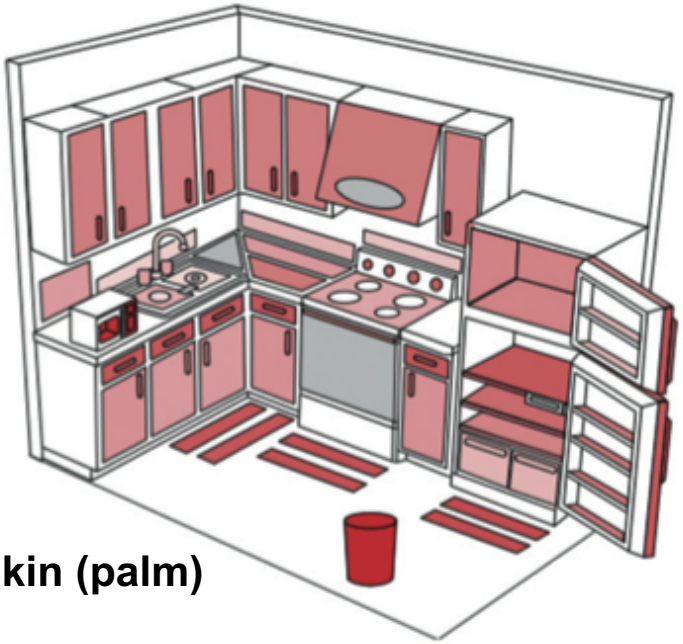
Two shopping centers in Singapore

Tringe et al. **2008** *PLoS ONE* 3:e1862

6. Source tracking techniques demonstrate that humans and pets often dominate bacterial communities on indoor surfaces

Diversity, distribution and sources of bacteria in residential kitchens

"Human skin was the primary source of bacteria across all kitchen surfaces, with contributions from food and faucet water dominating in a few specific locations"



Skin (palm)

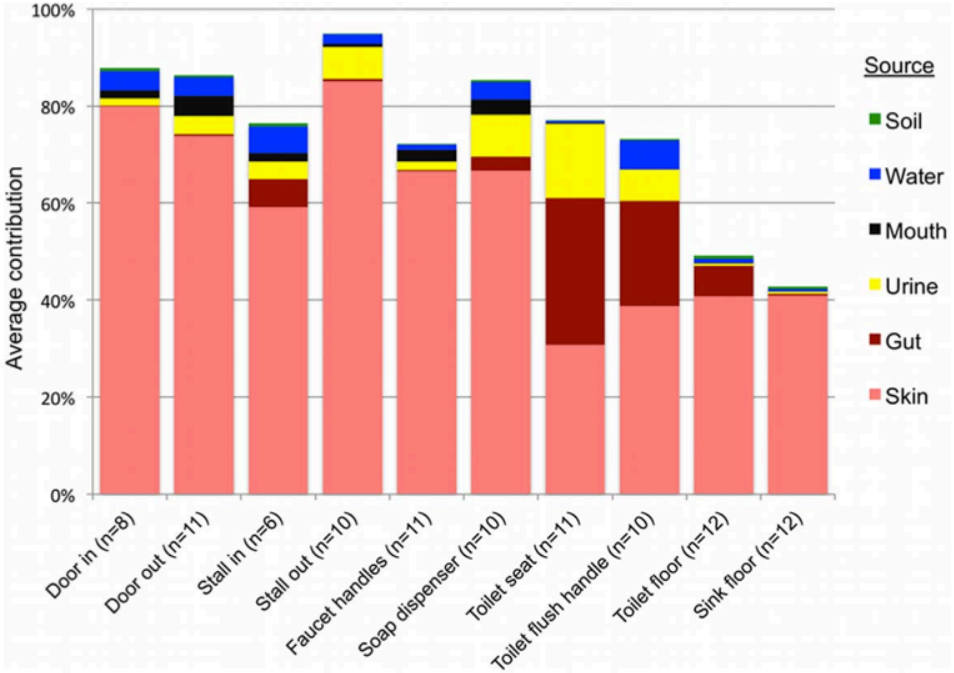
Flores et al. **2013** *Environ Microbio* 15:588-596

Microbial Biogeography of Public Restroom Surfaces

Gilberto E. Flores[1], Scott T. Bates[1], Dan Knights[2], Christian L. Lauber[1], Jesse Stombaugh[3], Rob Knight[3,4], Noah Fierer[1,5]*

"Human-associated microbes are commonly found on restroom surfaces"

"Bacterial pathogens could readily be transmitted between individuals by the touching of surfaces"



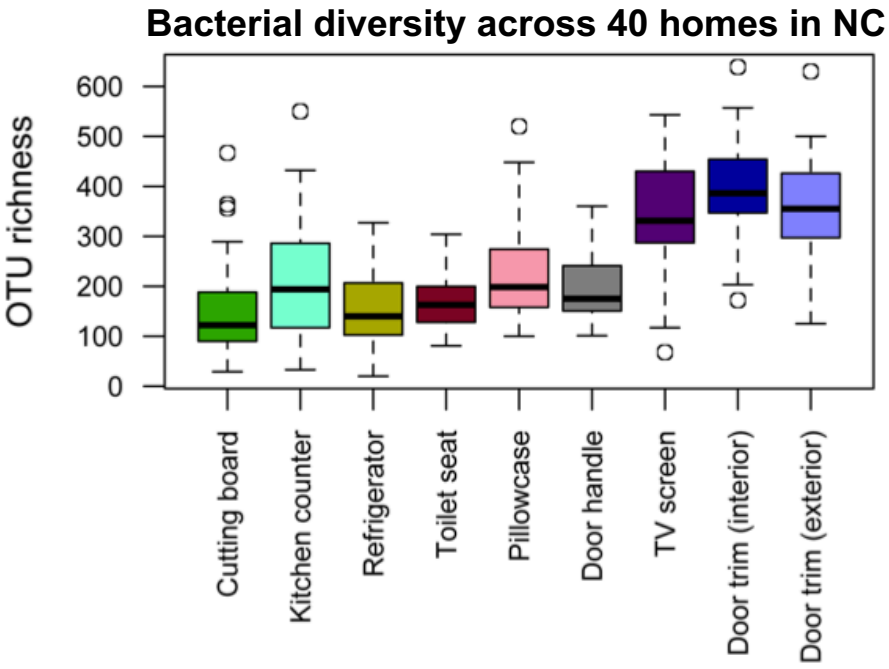
Flores et al. **2011** *PLoS ONE* 6(11):e28132

6. Source tracking techniques demonstrate that humans and pets often dominate bacterial communities on indoor surfaces

Home Life: Factors Structuring the Bacterial Diversity Found within and between Homes

Robert R. Dunn[1*], Noah Fierer[2,3], Jessica B. Henley[2], Jonathan W. Leff[2], Holly L. Menninger[1]

- Specific locations were distinct
- Presence of dogs → greater diversity
- Correlations between I and O communities

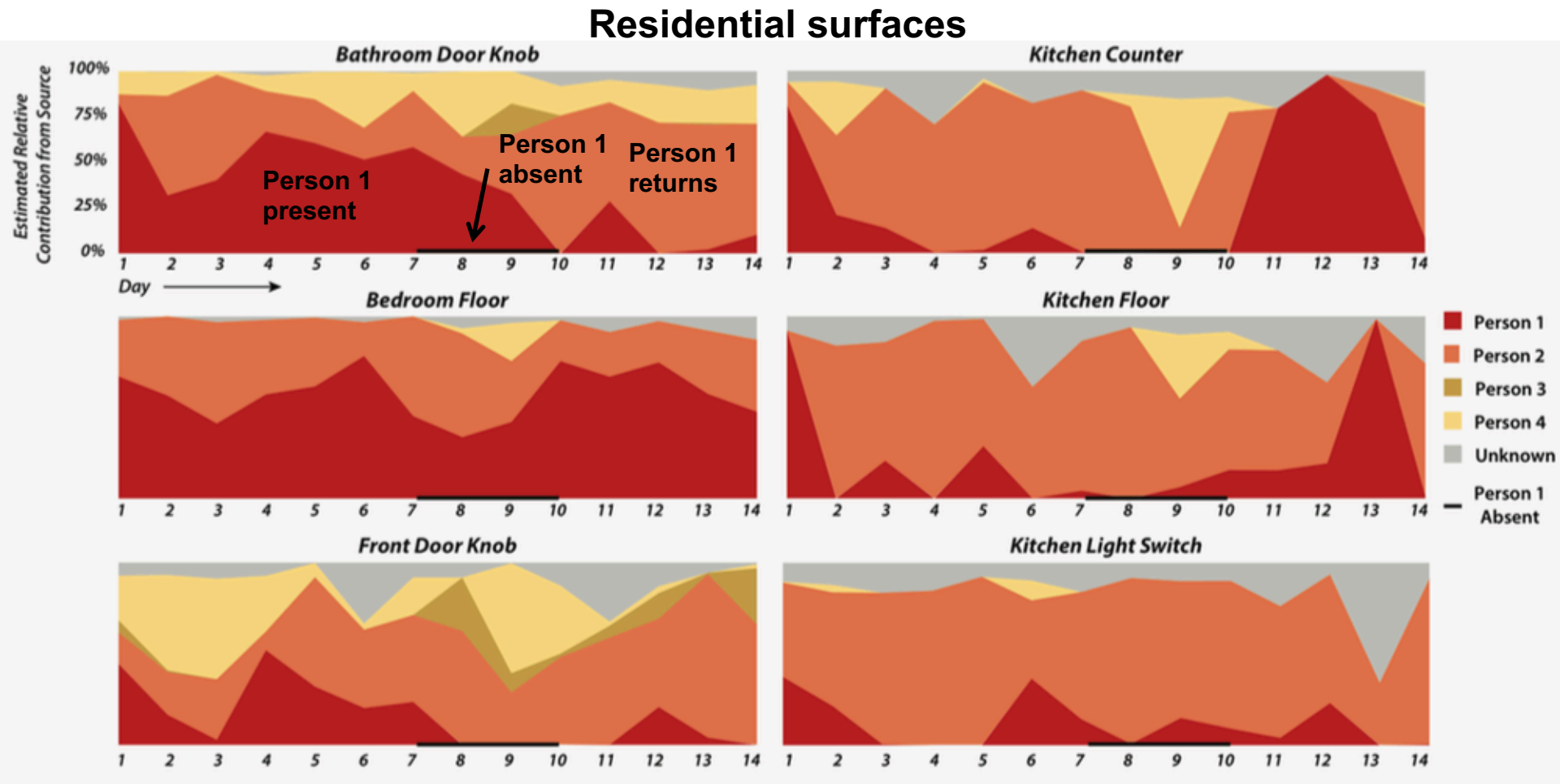


	Human skin	Human oral cavity	Human stool	Leaves	Soil
Cutting board	0.6	0.7	0.1	1.2	0.6
Kitchen counter	2.5	2.4	0.4	1.8	1.2
Refrigerator	2.0	1.3	0.2	1.1	0.7
Toilet seat	17.2	7.9	5.7	0.1	0.3
Pillowcase	9.3	24.2	1.3	0.6	0.7
Door handle	5.7	9.0	0.7	1.2	2.5
Television	7.9	6.4	1.9	1.7	3.3
Door trim (interior)	4.8	2.3	1.7	3.3	4.8
Door trim (exterior)	0.7	0.2	0.2	3.7	7.0

Figure 4. Source tracking analysis showing relative proportion of bacteria at each sampling site associated with given sources.

Dunn et al. **2013** *PLoS ONE* 8(5):e64133

6. Source tracking techniques demonstrate that humans and pets often dominate bacterial communities on indoor surfaces

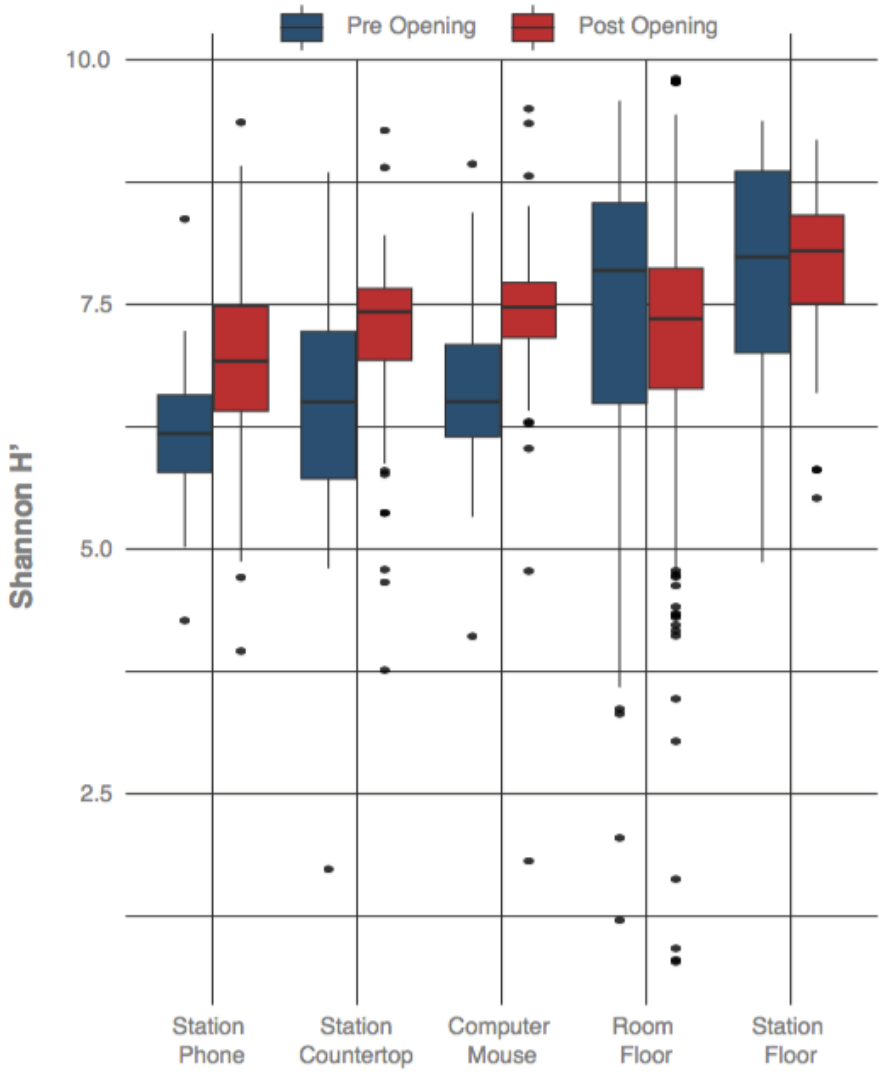


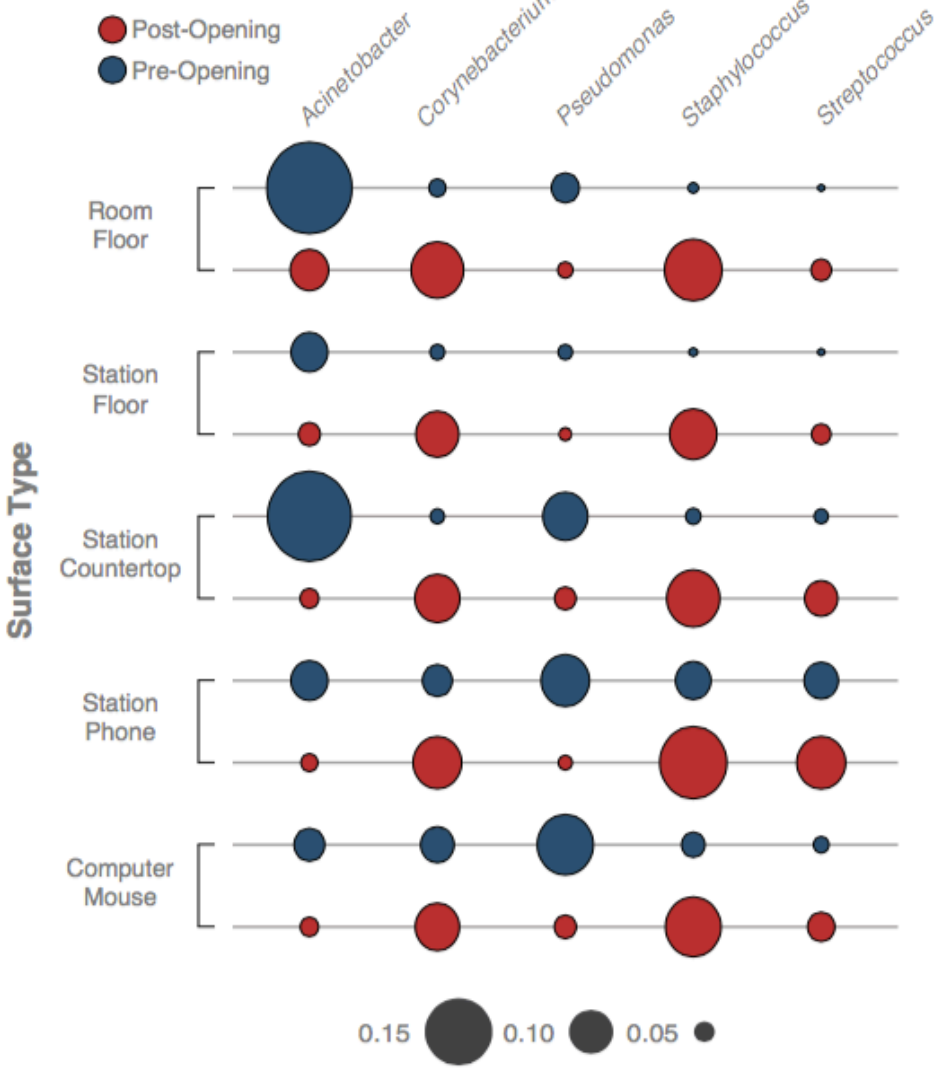
Also, after a move to a new house, the microbial community in the new house rapidly converges on the microbial community of the occupants former house

Lax et al. **2014** *Science* 345(6200):1048-1052

6. Source tracking techniques demonstrate that humans and pets often dominate bacterial communities on indoor surfaces

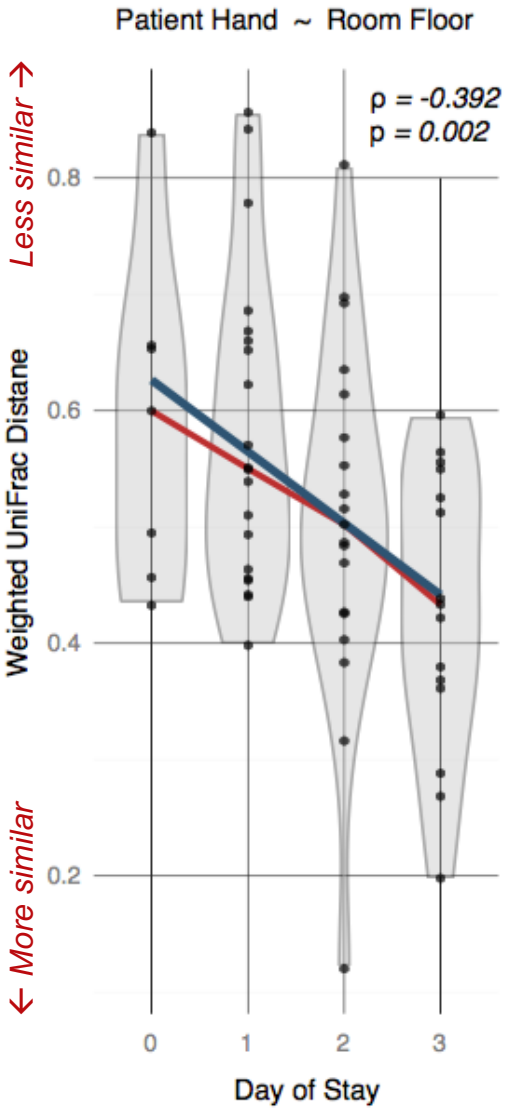
Hospital surfaces before and after opening





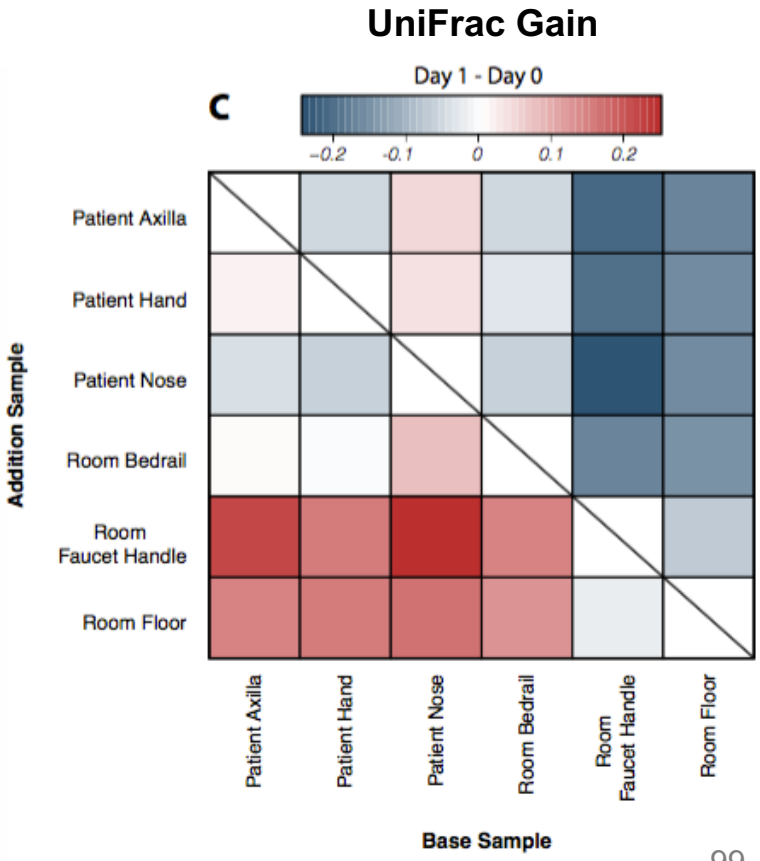
Lax et al. **2017** *Science Transl Med*

7. Occupants and surfaces interact in both directions



"…taxa shared with the skin of the current patient are more abundant on room surfaces after the patient has spent a night in the room, while taxa shared with room surfaces are more abundant on patient skin when a patient first enters the room"

"This asymmetry may suggest that patients initially pick up room-associated taxa that predate their stay, but that their own microbial signatures begin to influence the room with time."



Hospital Microbiome

Lax et al. **2017** *Science Transl Med*

8. Humans are also major sources of bacteria to indoor air

Human Occupancy as a Source of Indoor Airborne Bacteria

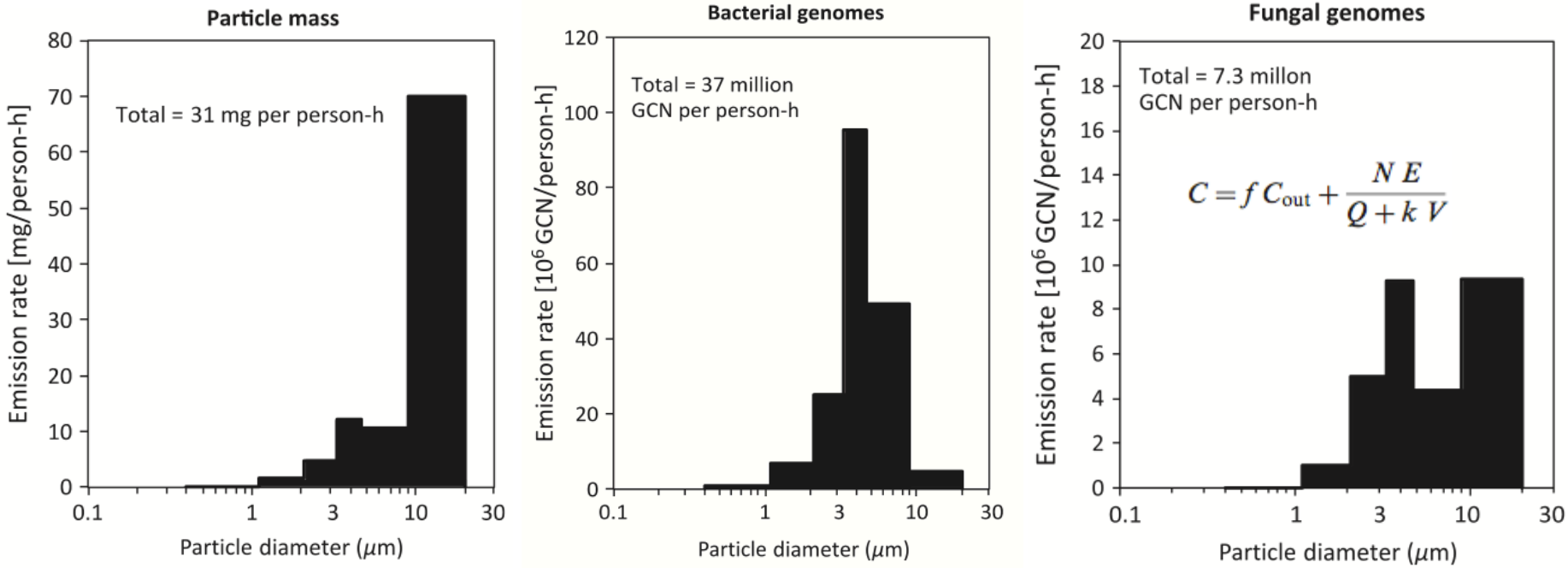
Denina Hospodsky[1], Jing Qian[1¤a], William W. Nazaroff[2], Naomichi Yamamoto[1,3], Kyle Bibby[1], Hamid Rismani-Yazdi[1¤b], Jordan Peccia[1*]

Hospodsky et al. **2012** *PLoS ONE* 7(4):e34867

"Occupancy increased the total aerosol mass and bacterial genome concentration in indoor air… with an increase of nearly two orders of magnitude in airborne bacterial genome concentration in PM_{10}"

Size-resolved emission rates of airborne bacteria and fungi in an occupied classroom

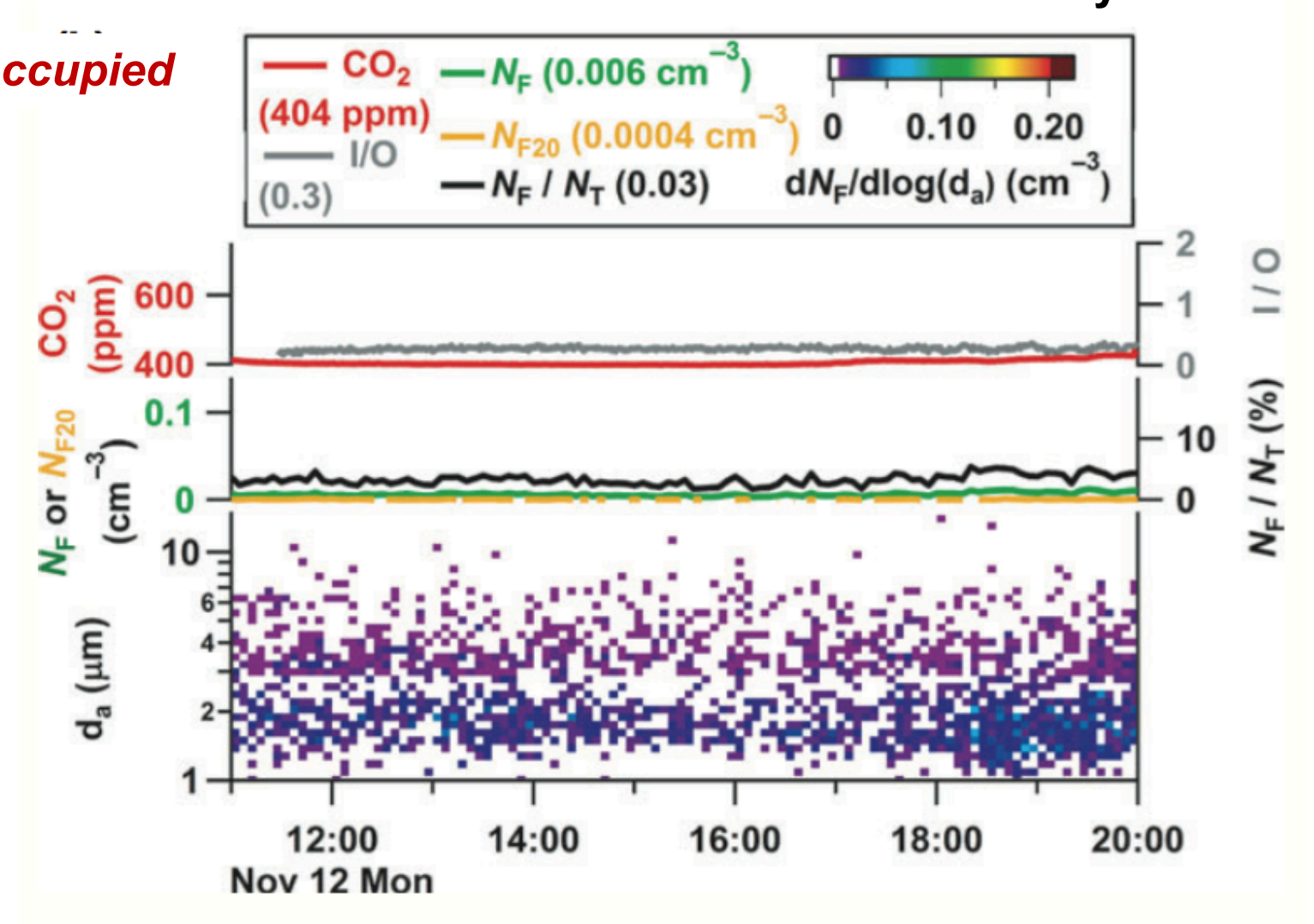
Qian et al. **2012** *Indoor Air* 22:339-351



8. Humans are also major sources of bacteria to indoor air

Classroom fluorescent bioaerosol study

Unoccupied

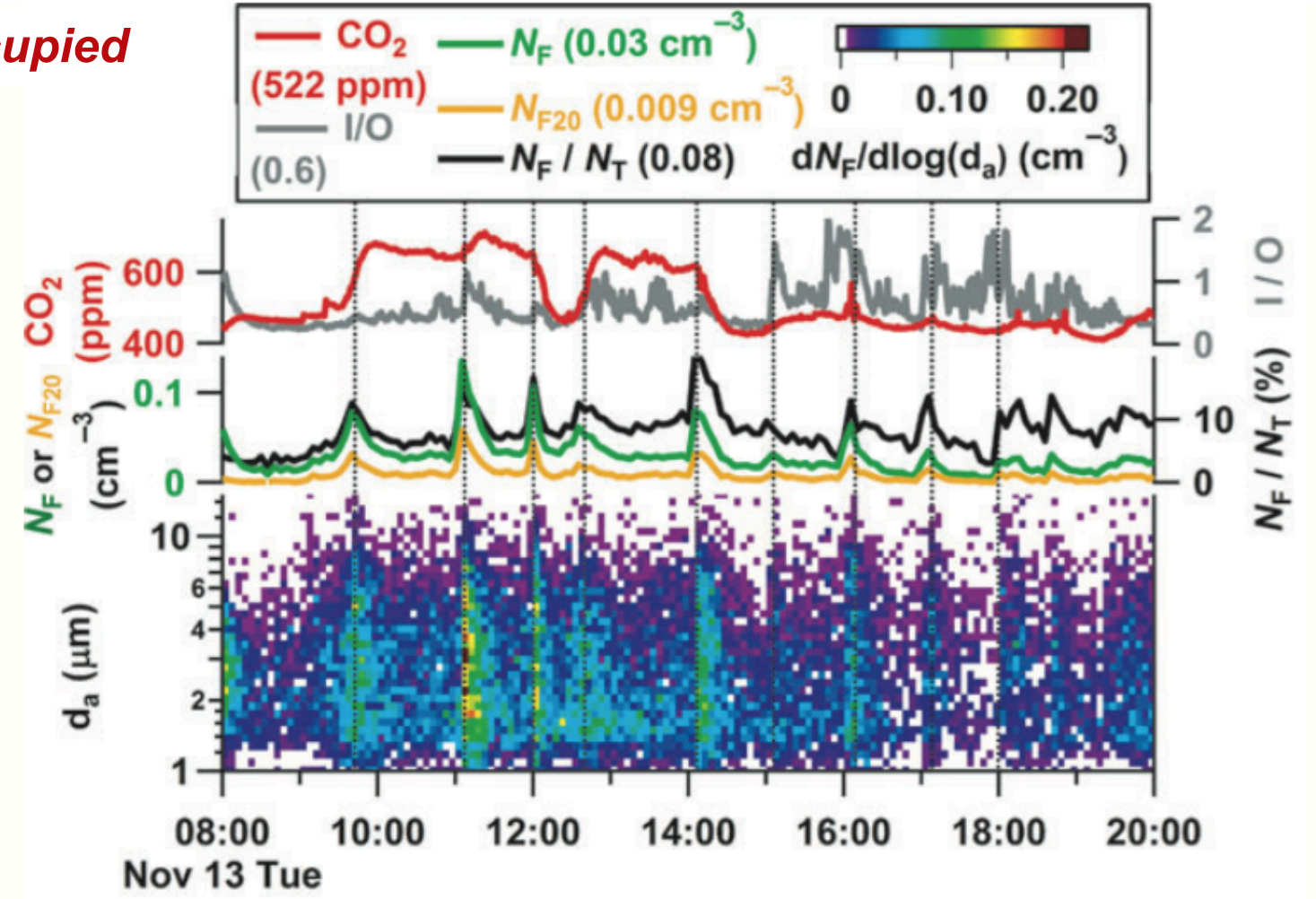


Bhangar et al. **2014** *Indoor Air* 24(6):604-617

8. Humans are also major sources of bacteria to indoor air

Classroom fluorescent bioaerosol study

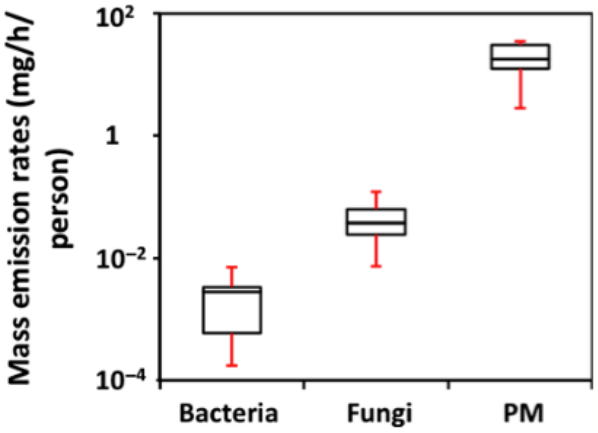
Occupied

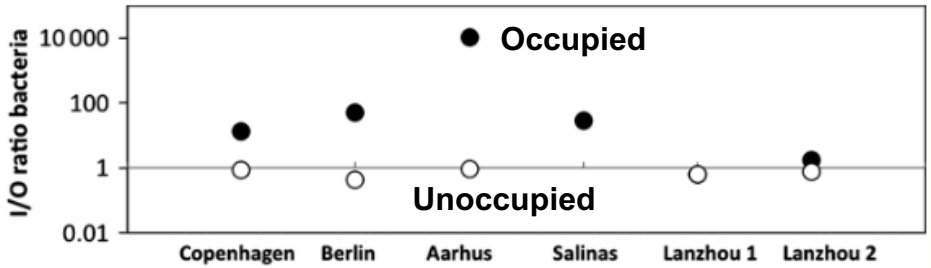


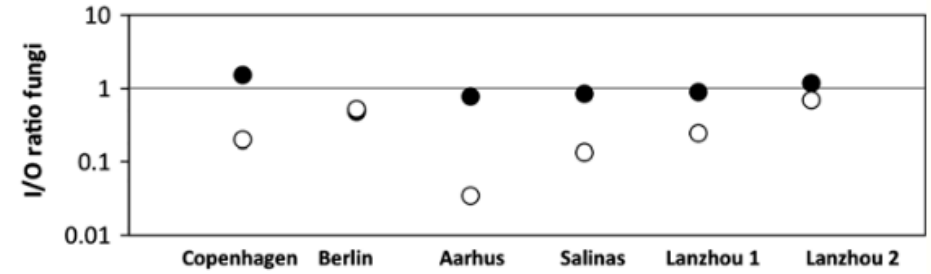
Bhangar et al. **2014** *Indoor Air* 24(6):604-617

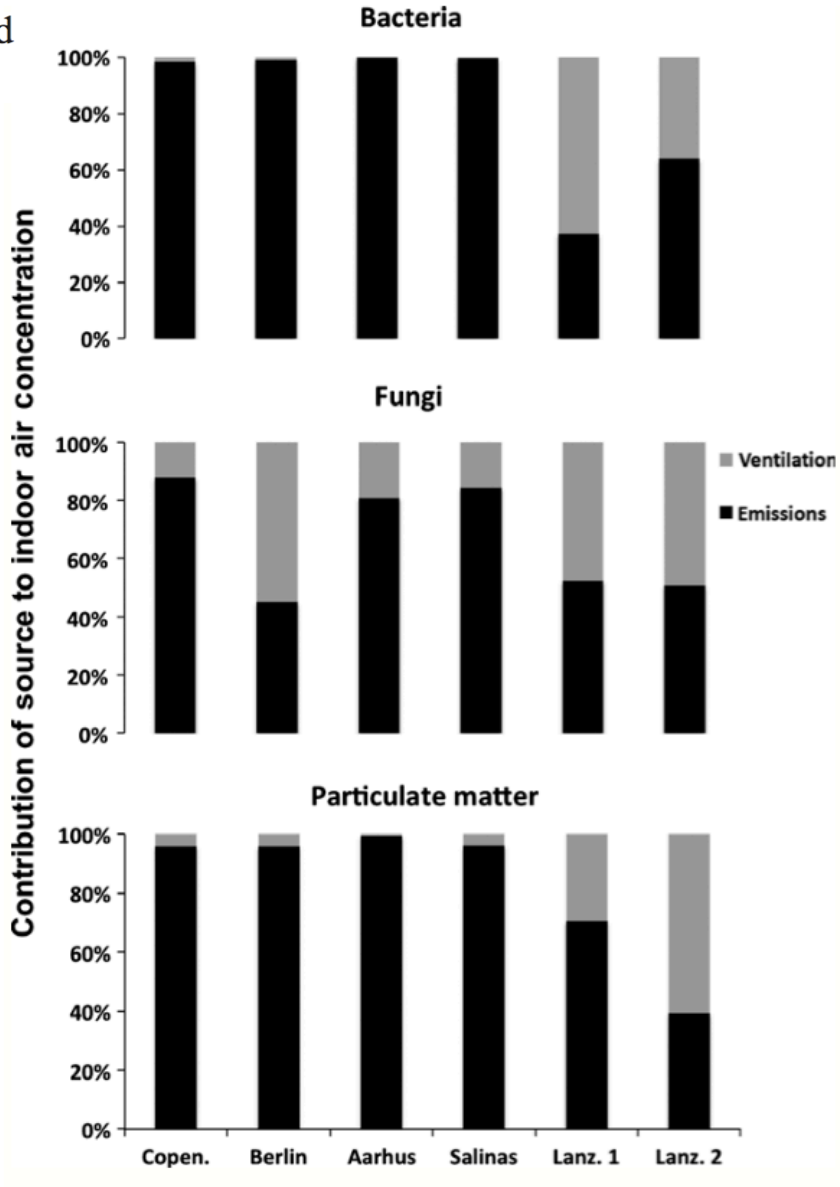
8. Humans are also major sources of bacteria to indoor air

Characterizing airborne fungal and bacterial concentrations and emission rates in six occupied children's classrooms







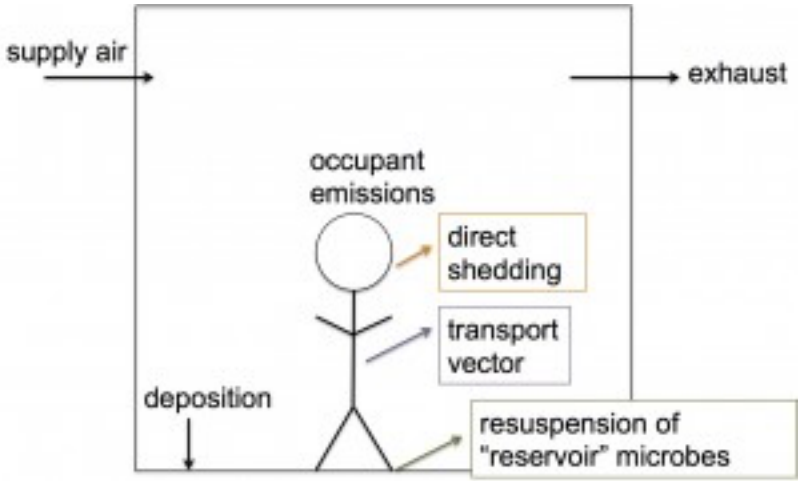


Hospodsky et al. **2015** *Indoor Air* 25:641-652

9. Controlled studies can elucidate the mechanisms of human microbial emissions

Mechanisms of human emissions:

1. Direct shedding
2. Resuspension of settled particles
3. Direct surface contact



Courtesy of Rachel Adams

Bhangar et al. **2016** *Indoor Air* 26(2):193-206

9. Controlled studies can elucidate the mechanisms of human microbial emissions

Mechanisms of human emissions:

1. Direct shedding
2. Resuspension of settled particles
3. Direct surface contact

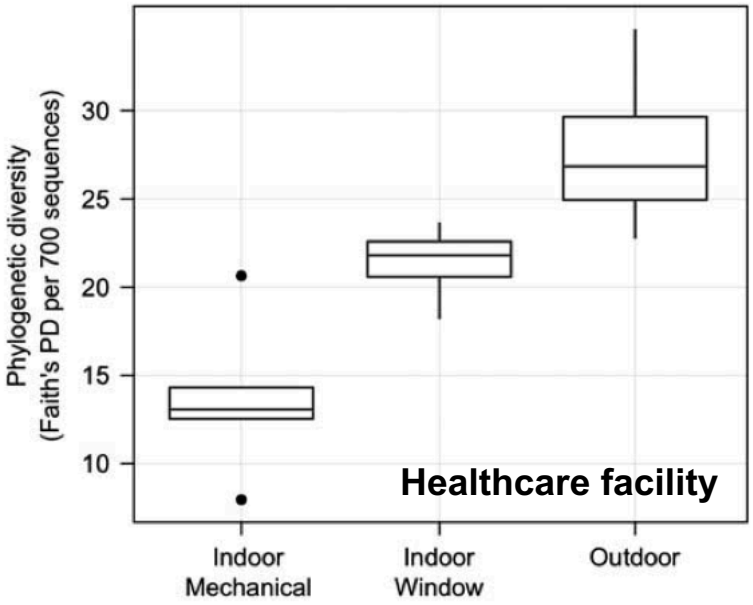
- Seated, simulated office work conditions: ~10^6 particles per hour per person
  - Fluorescence (UV-APS)
- Walking increased this 5-6x
  - Mostly attributable to resuspension
  - And some additional direct shedding (arm movements)
- During both walking and sitting, more than 65% of the emissions originated from the floor
  - Resuspension was dominant
- Dominant particle size: ~3-5 μm

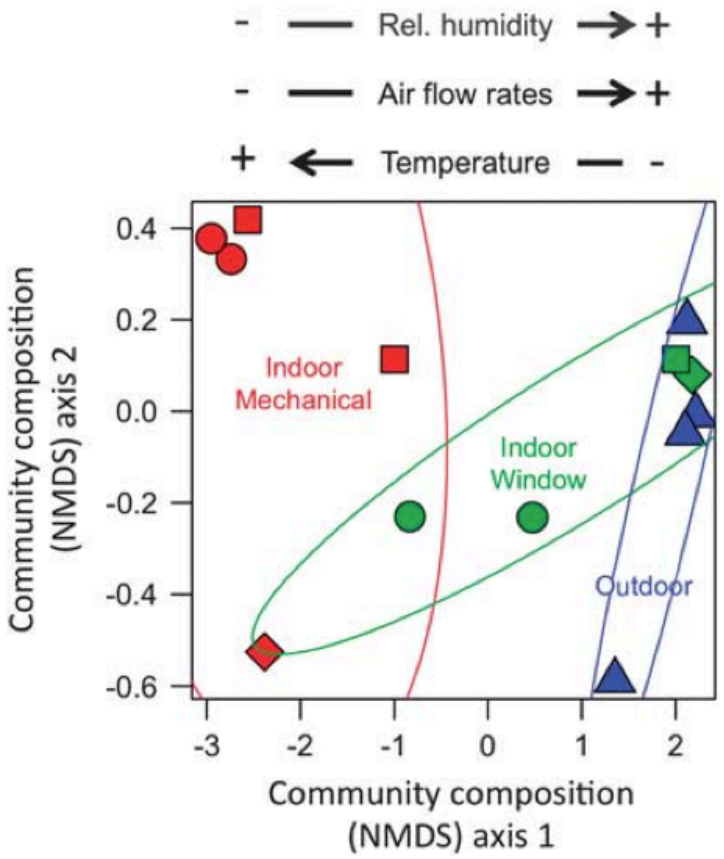
Bhangar et al. **2016** *Indoor Air* 26(2):193-206

10. Building design and operation can influence indoor microbial communities

Architectural design influences the diversity and structure of the built environment microbiome

Steven W Kembel[1], Evan Jones[1], Jeff Kline[1,2], Dale Northcutt[1,2], Jason Stenson[1,2], Ann M Womack[1], Brendan JM Bohannan[1], G Z Brown[1,2] and Jessica L Green[1,3]





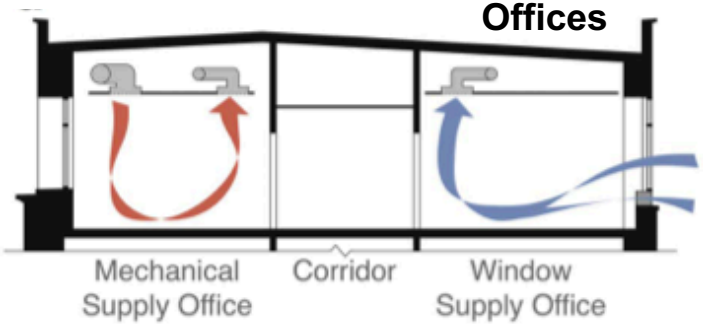
- Bacterial diversity: IA < OA
- Rooms w/ HVAC were less diverse than open window rooms
- Source of ventilation air and T/RH correlated w/ composition of IA bacteria

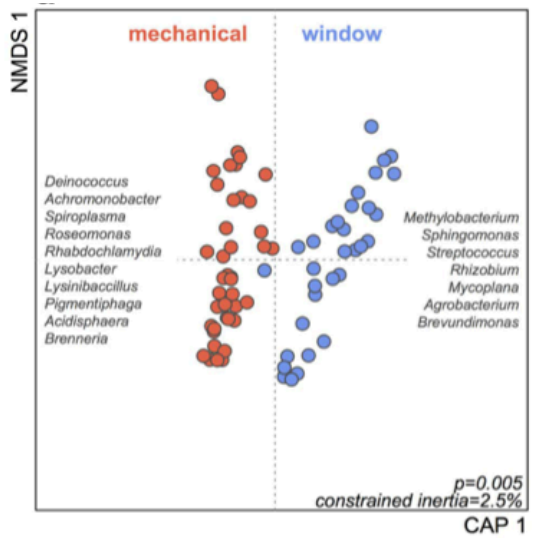
Kembel et al. **2012** *ISME J* 6:1469-1479

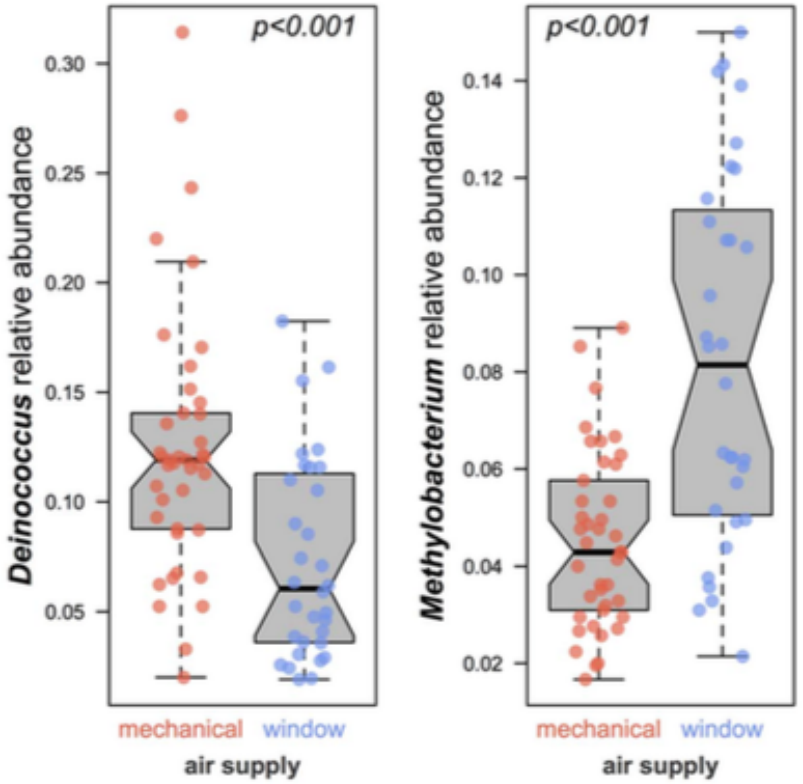
10. Building design and operation can influence indoor microbial communities

Architectural Design Drives the Biogeography of Indoor Bacterial Communities

Steven W. Kembel[1,2,3*], James F. Meadow[2,3*], Timothy K. O'Connor[2,3,4], Gwynne Mhuireach[2,5], Dale Northcutt[2,5], Jeff Kline[2,5], Maxwell Moriyama[2,5], G. Z. Brown[2,5,6], Brendan J. M. Bohannan[2,3], Jessica L. Green[2,3,7]







"Within offices, the source of ventilation air had the greatest effect on bacterial community structure"

- Even if absolute abundance remains similar

Kembel et al. **2014** *PLoS ONE* 9(1):e87093

10. Building design and operation can influence indoor microbial communities

Influence of housing characteristics on bacterial and fungal communities in homes of asthmatic children

"Increased microbial richness was associated with the presence of pets, water leaks, longer AC use, suburban (vs. urban) homes, and dust composition measures"

"The most significant differences in community composition were observed for AC use and occupancy (people, children, and pets) characteristics"

"Occupant density measures were associated with beneficial bacterial taxa, including *Lactobacillus johnsonii*"

Table 1 Richness analysis of housing characteristics for fungi and bacteria. Associations with $P < 0.05$ are in bold

		Mean number of fungal OTUs			Mean number of bacterial OTUs		
Category	*n* (yes)	Yes	No	*P*-value	Yes	No	*P*-value
More than 5 people in home	49	95.7	91.8	0.59	735	735	0.91
More than 3 children in home	87	96.6	91.8	0.54	701	743	0.26
Urban home (vs. Suburban)	112	90.1	96.2	0.33	**707**	**772**	**0.031**
Single family (vs. Multifamily)	94	92.8	92.6	0.98	755	717	0.22
Mold	85	94.0	91.8	0.73	738	728	0.75
Water leaks	80	**102**	**86.6**	**0.017**	729	740	0.73
AC use (yes or no)	178	92.6	94.4	0.86	737	712	0.63
AC use (more than 2 months)[a]	105	**86.6**	**102.4**	**0.021**	730	757	0.40
Pets	85	**101**	**86.2**	**0.015**	**772**	**704**	**0.024**

'Yes' and 'no' refer to the category, that is, for pets, 'yes' homes had pets and 'no' homes did not have pets.

[a]Excludes homes with no AC use.

Dannemiller et al. **2016** *Indoor Air* 26:179-192

10. Building design and operation can influence indoor microbial communities

RESEARCH ARTICLE

Fungal and Bacterial Communities in Indoor Dust Follow Different Environmental Determinants

Fabian Weikl[1]*, Christina Tischer[2,3], Alexander J. Probst[4], Joachim Heinrich[2,5], Iana Markevych[2,6], Susanne Jochner[7], Karin Pritsch[1]

Fungal communities in house dust (286 homes) impacted by:

- Surrounding greenness
- Outdoor PM concentrations
- Age of building
- Window opening behavior

Table 1. Significance of associations between environmental determinants and microbial community variation (based on Bray—Curtis dissimilarities).

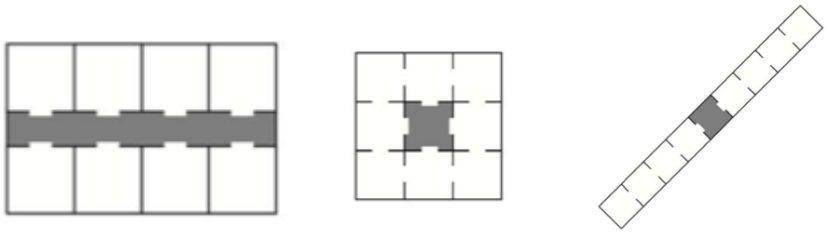
	Fungi		Bacteria	
Environmental characteristics	P^a	δ^b	P^c	δ^d
Indoor characteristics				
N° of rooms within the flat	0.75	0.87	0.71	0.79
N° of occupants in the flat	0.85	0.79	0.36	0.28
Dampness	0.69	0.29	0.16	0.39
Mould at home	**0.04**	**0.03**	0.09	0.13
Water leakage	0.81	0.85	0.57	0.62
Tightness of the windows [e]	**0.03**	**0.04**	0.36	0.36
Ventilation living room through windows—summer	0.27	0.24	0.71	0.93
Ventilation living room through windows—winter	0.67	0.64	**0.05**	**0.05**
Heating within the home	**0.03**	**0.02**	0.36	0.41
Renovation measures last 12 months	0.44	0.61	0.65	0.65
Pets	0.27	0.28	0.62	0.75
Type of living room floor	**< 0.001**	**< 0.001**	0.08	**0.02**
Smoking of tobacco in the flat	0.42	0.41	0.71	0.78
Outdoor characteristics				
Age of the building	**0.01**	**0.01**	0.28	0.31
Position of the home	0.49	0.67	0.1	**0.05**
Building density of the neighbourhood	0.52	0.59	0.39	0.44
Traffic jams in rush hour	0.83	0.83	0.29	0.24
Facility with noticeable air pollution within 50 and 100 m	0.58	0.72	0.45	0.40
Facility with noticeable air pollution within 50 m	0.33	0.28	0.85	0.94
Surrounding greenness (500 m buffer)	0.72	0.63	084	0.94
Surrounding greenness (100 m buffer)	**0.05**	**0.006**	0.19	0.22
Surrounding greenness (30 m buffer)	0.06	**0.01**	0.33	0.30
Urban index	**0.02**	**0.01**	0.51	0.60
NO_2	0.23	0.06	0.63	0.75
NO_x	0.06	**0.03**	0.37	0.41
$PM_{2.5}$	**0.004**	**0.005**	0.51	0.44
PM_{10}	0.54	0.32	0.82	0.70
PM_{coarse}	**0.04**	**0.008**	0.41	0.46
$PM_{2.5}$ absorbance	0.07	0.06	0.37	0.42

Weikl et al. **2016** *PLoS ONE* 11(4):e0154131

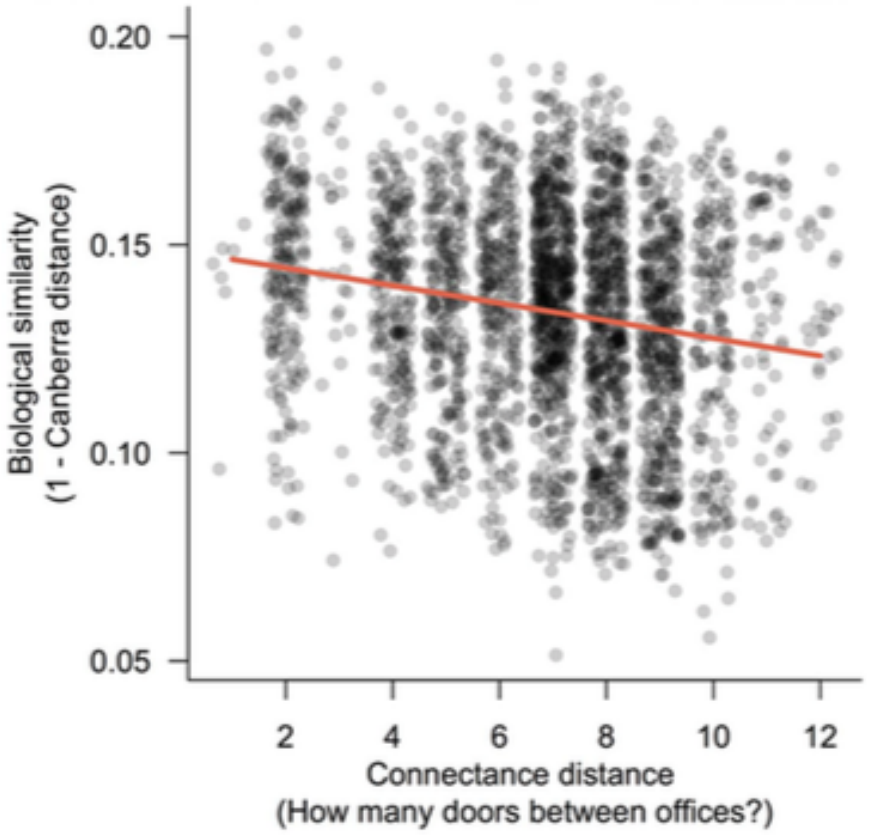
10. Building design and operation can influence indoor microbial communities

Architectural Design Drives the Biogeography of Indoor Bacterial Communities

Steven W. Kembel[1,2,3*], James F. Meadow[2,3*], Timothy K. O'Connor[2,3,4], Gwynne Mhuireach[2,5], Dale Northcutt[2,5], Jeff Kline[2,5], Maxwell Moriyama[2,5], G. Z. Brown[2,5,6], Brendan J. M. Bohannan[2,3], Jessica L. Green[2,3,7]



"Spaces with high human occupant diversity and a high degree of connectedness to other spaces via ventilation or human movement contained a distinct set of bacterial taxa when compared to spaces with low occupant diversity and low connectedness"



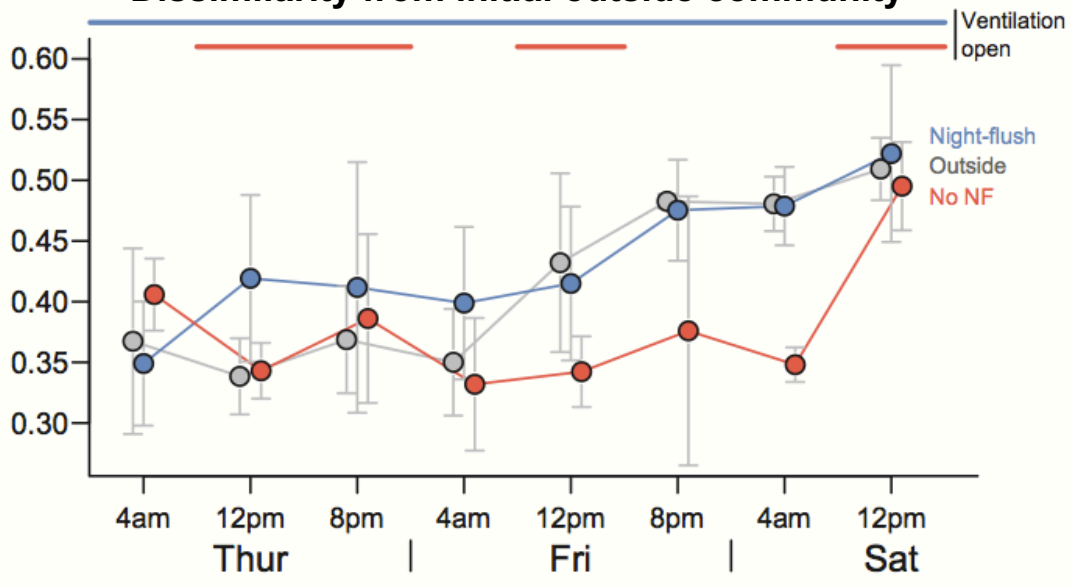
Kembel et al. **2014** *PLoS ONE* 9(1):e87093

10. Building design and operation can influence indoor microbial communities

Indoor airborne bacterial communities are influenced by ventilation, occupancy, and outdoor air source

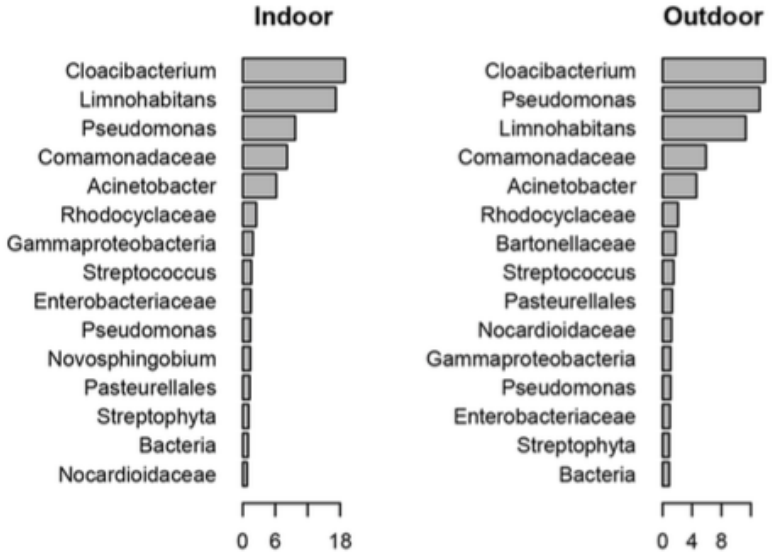
- Indoor air communities closely tracked OA
- Human-associated bacterial genera were more than 2x as abundant in IA vs. OA
- Ventilation had a demonstrated effect on indoor airborne bacterial community composition (following a time lag)

Dissimilarity from initial outside community



Meadow et al. **2013** *Indoor Air* 24(1):41-48

Another chamber study (bacteria):

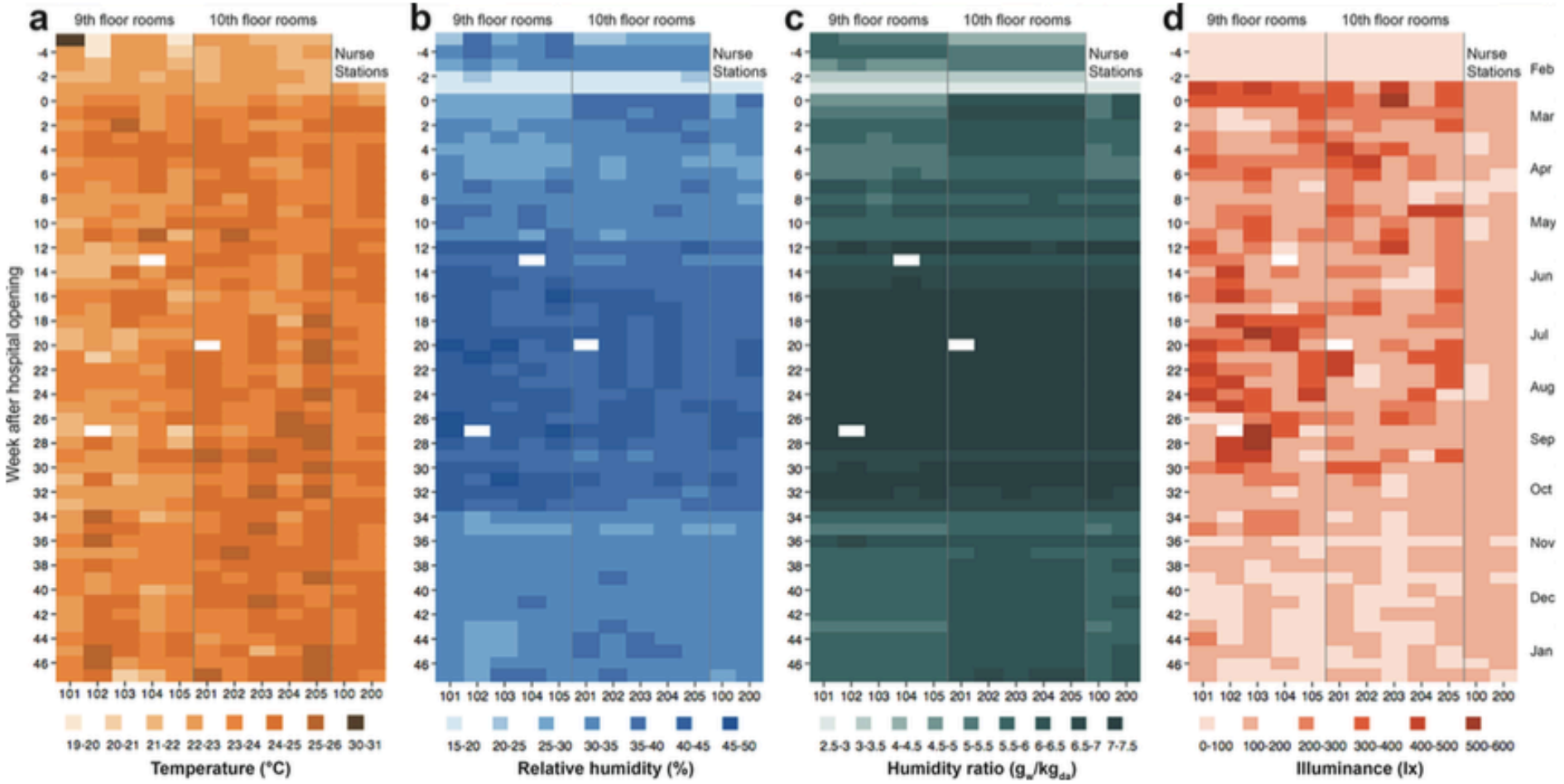


- In a mechanically ventilated office setup (~3 ACH and MERV 7 filtration), indoor microbial composition mostly tracked that of outdoor composition
  - The number of occupants and their activity had a smaller influence on indoor bioaerosol composition than expected

Adams et al. **2015** *PLOS ONE* 10(5):e0128022

11. Building environmental conditions often have a small influence on indoor microbial communities

Long-term environmental conditions in a new hospital

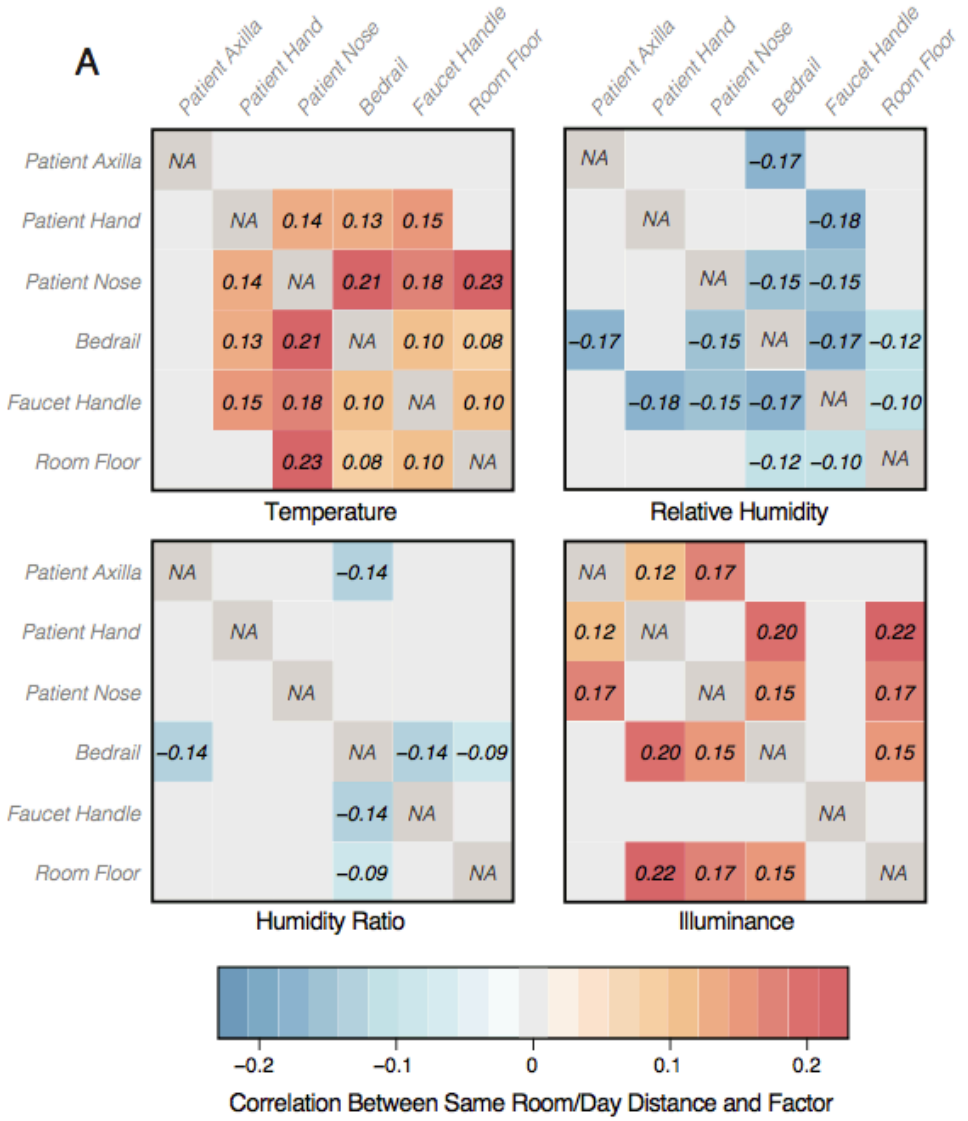


Ramos et al. **2015** *PLOS ONE* 10(3):e0118207

11. Building environmental conditions often have a small influence on indoor microbial communities

Bacterial community similarity and long-term environmental conditions in a new hospital

"…higher temperatures and higher illuminance were consistently associated with greater microbial dissimilarity between patient and surface microbial communities, while higher relative humidity and humidity ratio were consistently correlated with greater microbial similarity"

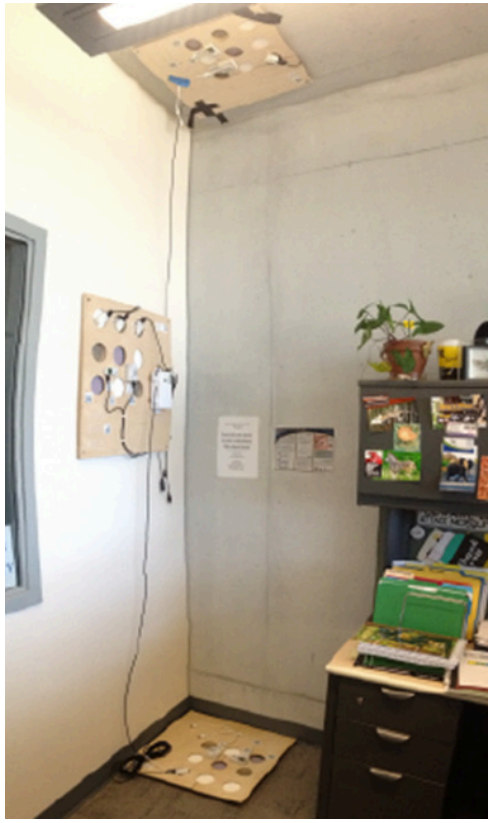


Lax et al. **in review**

11. Building environmental conditions often have a small influence on indoor microbial communities

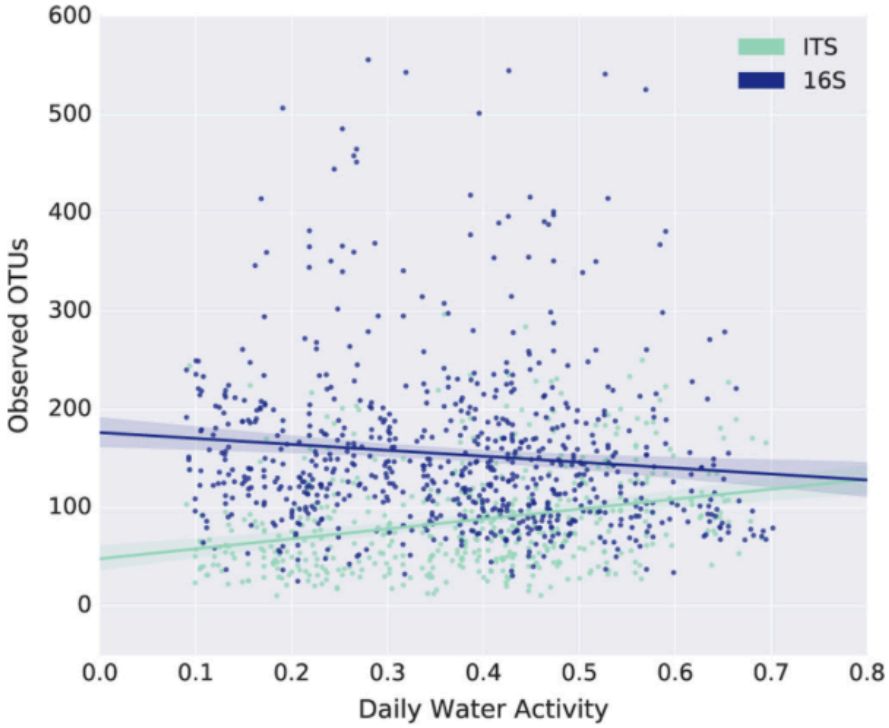
The Built Environment Is a Microbial Wasteland

Gibbons **2016** *mSystems*



Geography and Location Are the Primary Drivers of Office Microbiome Composition

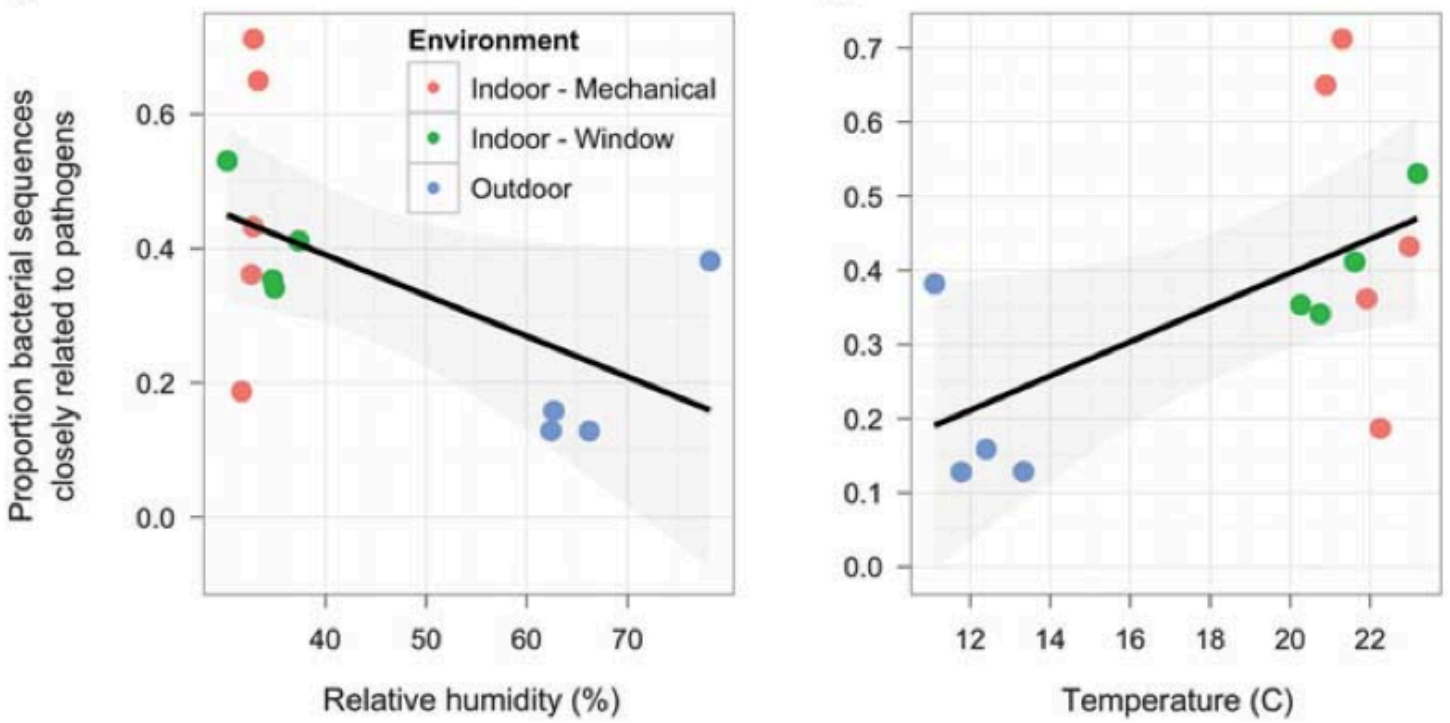
Chase et al. **2016** *mSystems* 1(2):e00022-16



11. Building environmental conditions often have a small influence on indoor microbial communities

Correlations of bacterial findings with environmental conditions in a hospital room

*Factors are correlated



Kembel et al. **2012** *ISME J* 6:1469-1479

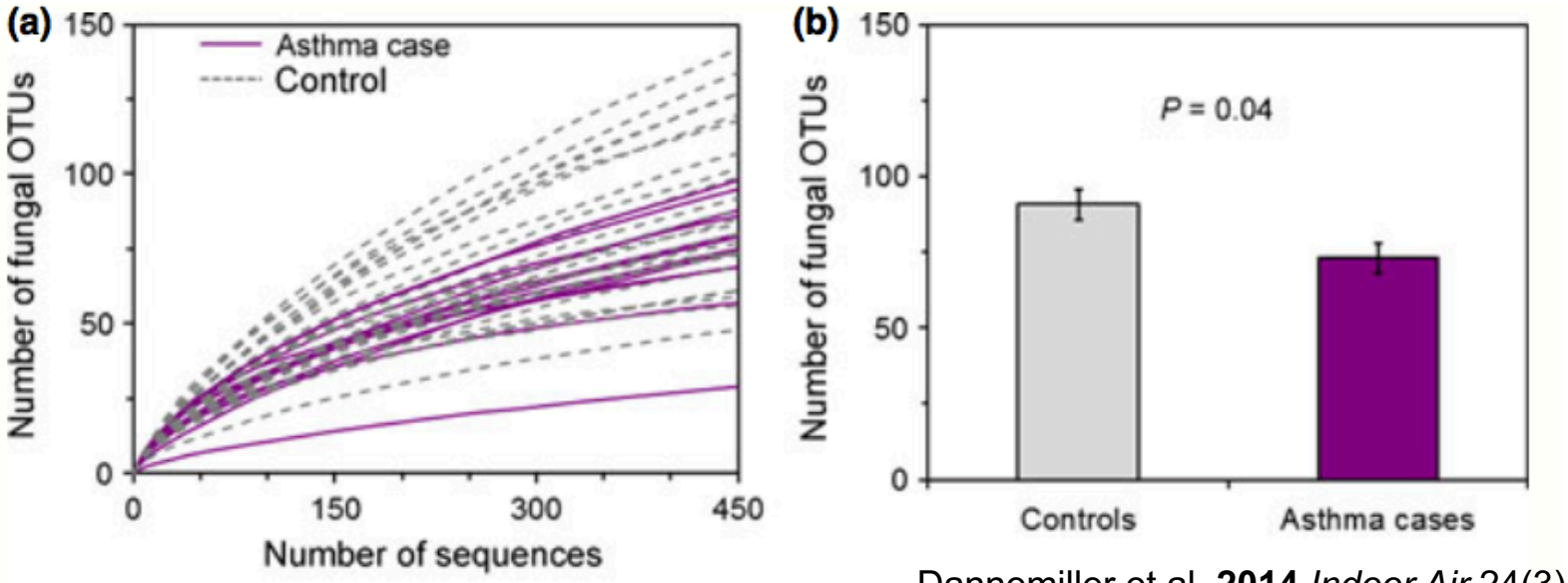
Correlations of bacterial findings with homes characteristics

"Bacterial richness tended to be higher in those four (of 11) units that reported at least occasional humidifier use"

Adams et al. **2014** *PLoS ONE* 9(3):e91283

12. Exposures to microbial diversity (i.e., the 'right' number of the 'right' kinds of microbes) can be beneficial for health

Next-generation DNA sequencing reveals that low fungal diversity in house dust is associated with childhood asthma development



Dannemiller et al. **2014** *Indoor Air* 24(3):236-247

Effects of early-life exposure to allergens and bacteria on recurrent wheeze and atopy in urban children

"…children with the highest exposure to specific allergens and bacteria during their first year were least likely to have recurrent wheeze and allergic sensitization"

Lynch et al **2014** *J Allergy Clin Immunol* 134:593-601

Summary of (some of) what we have learned

1. Culture-independent methods reveal vastly greater microbial diversity compared to culture-based methods
2. Indoor spaces often harbor unique microbial communities
3. Indoor fungal communities are largely driven by outdoor fungal communities (in non-damp buildings)
4. Indoor fungal communities in damp buildings are often distinct from those in non-damp buildings
5. Indoor bacteria often originate from indoor sources
6. Source tracking techniques demonstrate that humans and pets often dominate bacterial communities on indoor surfaces
7. Occupants and surfaces interact in both directions
8. Humans are also major sources of bacteria to indoor air
9. Controlled studies can elucidate the mechanisms of human microbial emissions
10. Building design and operation can influence indoor microbial communities
11. Building environmental conditions often have a small influence on indoor microbial communities (but sometimes larger)
12. Exposures to microbial diversity (i.e., the ‘right’ number of the ‘right’ kinds of microbes) can be beneficial for health

From 1887 to 2016 and beyond

"The combination of culture and culture-independent methods provided powerful means for determining both viability and diversity of bacteria in child-care facilities."

"Although our study identified a remarkable array of microbial diversity present in a single daycare, it also revealed just how little we comprehend the true extent of microbial diversity in daycare centers or other indoor environments."

Lee et al. **2007** *BMC Microbiology* 7:27

How will we change the way we design and operate buildings?

New Sherwin-Williams paint kills infection-causing bacteria

Nathan Bomey, USA TODAY 7:07 a.m. EDT October 28, 2015

Can bioinformed design promote healthy indoor ecosystems?

Jessica L. Green
University of Oregon

?

Antibiotic ← → **Probiotic**

The “wrong” microbes

The “right” microbes