Exposure Assessment Strategies in Occupational and Environmental Epidemiology

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Overview of Presentation

- Societal and scientific context of occupational and environmental epidemiology research
- Exposure assessment tools: questionnaires, expert evaluation, environmental measurements, GIS, personal measurements, biological measurements
- Examples: residential EMF, occupational EMF, drinking water disinfection by-products
- Recommended approach to exposure assessment

Exposure Assessment Challenges and Opportunities

- Limiting factor in validity of occupational and environmental epidemiology research
- Distinct methodologic issues in workplace compared to community/home environments
- Occupational exposures traditionally higher and better documented, but more demographically restricted populations

Societal Context for Occupational & Environmental Epidemiology

- Deep concern with protection from harm relative to other influences on health
  - Public will to support research
  - Demonstrated adverse effects lead to regulation
  - Regulation requires monitoring data, benefits research
- Implications of research makes findings contentiousness
  - Distortion for political/economic purposes
  - Demand for epidemiologic proof to justify action

Challenges in Occupational & Environmental Exposure Assessment

- Accurate, direct self-report is rarely possible – exposures involuntary, rarely perceptible, details difficult to recall
- Availability of crude indicators (job title, location) proliferates weak studies, improvements difficult
- Occupational exposures often confounded with other aspects of job (self-selection, selection for employment) and lifestyle correlates
- Environmental exposures confounded with residential location (socioeconomic)

Selection of Exposure Assessment Strategy

- Need overall model of potential etiologic process – how exposure may lead to disease (source, pathways, timing, biologic response)
- Assessment of validity requires specification of "gold standard" – quality of methods dependent on specific etiologic scenario
- Agent: specific chemical/physical exposure, source, pathway(s) to reaching humans, short-term and long-term variation

Selection of Exposure Assessment Strategy, cont.

- Health outcomes: specific entity, frequency of occurrence, ability to recognize onset, requirements for diagnosis
- Temporal relationship between exposure and health outcome
  - Duration of exposure required to cause disease – acute or chronic exposure
  - Importance of short-term and long-term variation in exposure
  - Interval between exposure and manifestation of outcome (latency)

Questionnaires/Self-Report

- Recall can be comprehensive
  - Report on all sources
  - Cover all time periods of interest
  - Includes behaviors that influence exposure
- Subject to error
  - Erroneous or incomplete recall
  - Biased recall related to health experience or beliefs
  - Susceptible to minor variation in wording or interviewer presentation

Expert Assessment & Inference

- Use knowledge of pollutant source and transport to estimate exposures
- Link accurately self-reported information to inferred exposure – job title, duties, locations, residential location, time-activity patterns
- Objective, integrate technical information and other experts, field work to refine or validate estimates
- Limited by incomplete self-report and source data, historical changes, dependence on individual experts

Environmental Measurements

- Routinely collected and archived measurements for regulatory purposes
  - Inexpensive, cover historical periods
  - Non-random sampling – worst case, dictated by regulations, arbitrary
  - Fixed locations of convenience, not necessarily where people spend time
  - Not collected for exposure assignment

Environmental Measurements, cont.

- Environmental area sampling for research
  - Choose locations with intent to characterize exposures for epidemiologic study
  - Allocate samples proportionate to intensity of exposure, variability, number of people
  - May be expensive, demanding of staff time, require direct access
  - Limited to current exposures

Geographic Information Systems

- Marked advancements in data availability, technology for linkage
- Dependent on degree to which location alone determines exposure – rarely sufficient
- Subject to overinterpretation
  - Location “causes” disease
  - Elegant technology applied to inherently limited data
- Subject to false negative implications
  - Inaccurate as “screening” method

Personal Measurements

- Assess exposure of individuals, incorporating variability in time-activity patterns
- Opportunity to study link between exposure determinants and measured exposure
- Use information on determinants to extrapolate beyond those sampled
- Expensive, often burdensome – only feasible for short-term exposure
- Dependent on available technology

Biological Measurements

- Measure of internal dose
  - Closer to health consequences
  - More distant from environmental exposure (influenced by metabolic differences, other contributors to dose)
- Integrates across exposure sources
  - Obviates need to measure sources
  - Loss of information on exposure sources, unclear implications for regulation

Biological Measurements, cont.

- Time period reflected by biomarker often shorter than desired
  - Subject to random error due to short interval
  - Subject to distortion by disease process (in case-control studies)
- Developmental research required to demonstrate validity for epidemiologic studies
  - Specimen collection, storage, and processing protocols
  - Sensitivity and specificity to environmental exposure of interest

Residential Magnetic Fields and Childhood Cancer

- Rarity of childhood cancer (~1 in 10,000 children per year) dictates case-control design
- Requires retrospective exposure assessment
  - Identify homes of interest
  - Characterize magnetic field exposure in homes using parental recall, archival data, or direct assessment
  - All *current* information needs to be extrapolated to *past* periods of interest

Magnetic Fields & Childhood Cancer – Exposure Source

- Home exposures determined primarily by current flow *past* the home, also in-home wiring, appliance placement and use
- Line phases should cancel, but separation in space and imbalance due to ground return result in fields proportionate to current
- Magnetic fields not easily shielded– power line characteristics reflect current flow, proximity to home determines magnitude

Residential Magnetic Fields and Childhood Cancer – Wire Codes

- Wire codes developed by Wertheimer & Leeper
- Ordinal ranking of exposure based on external power line characteristics and proximity to home
- Relegates all influences not captured as “noise” – in-home wiring, appliances, etc.
- Empirically associated with measured magnetic fields near homes

Residential Magnetic Fields & Childhood Cancer – Measured Fields

- In-home measurements reflect present, instantaneous levels accurately but interest is in past, stable levels
- Seek measurements that capture historically stable determinants, avoid short-term perturbations that are not generalizable
- Developed protocol for measurement (engineers, biophysicists, epidemiologists)

Residential Magnetic Fields & Childhood Cancer – Measured Fields

- Standardized choice of room locations – child's bedroom, common living area, next most occupied room (based on interview)
- Center of room, 1 meter high, away from appliances – avoid unstable influences
- Low power use to reflect background, high power use to reflect incremental contribution from electricity use

Residential Magnetic Fields in Relation to Wire Codes

	Wire Configuration Code				
	Buried	Very Low	Low	High	Very High
Low power mean (uT)	0.049	0.053	0.071	0.122	0.212
High power mean (uT)	0.060	0.077	0.109	0.161	0.292

Results for Wire Codes & Childhood Cancer

- Substantial attrition for in-home measurements due to moving from past residence, refusals
- Wire codes completed even for refusals
- 5-level wire code at diagnosis:
  - OR = 1.0 (referent), 1.6, 1.0, 1.5, 2.2 with increasing exposure
- High vs. low wire code:
  - Total Cancer -- OR = 1.5 (1.0-2.3)
  - Leukemia – OR = 1.5 (0.9-2.6)
  - Brain Cancer – OR = 2.0 (1.1-3.8)

Results for Measured Magnetic Fields & Childhood Cancer

- Low power magnetic fields and total childhood cancer:

  Exposure >0.2 uT -- OR = 1.4 (0.7-2.9)

  Exposure >0.3 uT-- OR = 2.3 (0.8-7.3)

- Low power magnetic fields and leukemia

  Exposure >0.2 uT -- OR = 1.9 (0.7-5.6)

  Exposure >0.3 uT -- OR = 3.7 (0.9-14.8)

Current Status of Evidence on Wire Codes & Childhood Cancer

- Pooled analysis indicates substantial heterogeneity across studies, ORs range from 0.7-3.0
- Early associations possibly due to patterns of non-response by social class
  - Case participation modestly increased among those of upper SES
  - Control participation markedly increased among those of upper SES

Current Status of Evidence on Magnetic Fields & Childhood Cancer

- Pooled analysis of 15 studies (Greenland et al., 2000)
- Magnetic fields results (12 studies)

Level (uT)	OR	95% CI
<0.1	1.0 (referent)	
0.1 - <0.2	1.0	0.8-1.2
0.2 - <0.3	1.1	0.8-1.4
>0.3	1.7	1.2-2.3

Current Status of Evidence on Magnetic Fields & Childhood Cancer

- Uncertainty in exposure assessment remains limiting factor despite advancements
- Consistent evidence of increased risk >0.3 uT, not below that level
- If true threshold, very limited impact – attributable fraction of ~3% in US; 1% of homes >0.4 uT
- Question of causality versus selection bias remains unresolved, perhaps unresolvable

Occupational Magnetic Fields and Adult Cancers

- Cohort study of electric utility workers focused on leukemia and brain cancer (very large population)
- Spectrum of jobs in industry, including many with low exposure
- Cohort from 5 large companies in US
- Goal: Define homogeneous exposure groups based on job titles, quantify exposure to allow integration across jobs, link to work history

Occupational Magnetic Fields and Adult Cancers, cont.

- Industrial processes stable throughout period of interest
- Job tasks stable but mix of activities and administrative titles varied by company, changed over time
- Learn about nature of work and specific jobs through site visits, discussion with managers and long-term workers, understanding sources of magnetic field exposure

Occupational Magnetic Fields and Adult Cancers -- Sampling

- Need and resources to conduct large-scale, random sampling of present-day workers to quantify magnetic field exposures
- Wrist monitor to measure exposure
- Sought random sample of worker-days for selected job titles at each company, some repeat measurements
- Oversample jobs with greater prevalence, higher exposure, and more variable exposure to characterize mean and median by job group

Occupational Magnetic Fields and Adult Cancers -- Measurements

- Challenges
  - Company/worker cooperation
  - Acceptance of true random sampling
- Products
  - Quantitative estimate of mean, median, and variability of exposure in each job group
  - Characterize at level of worker, job title, job group, and total

Occupational Magnetic Fields and Adult Cancers -- Measurements

Occ'l Category	#	Mean (uT)	Median (uT)
Linemen	251	0.65	0.23
Electrician	264	1.11	0.45
Cable splicers	149	1.50	0.40
Substation opr	84	0.80	0.41
Mechanics	100	0.23	0.15
Machinists	138	0.72	0.26
Admin. support	65	0.25	0.14

Occupational Magnetic Fields and Adult Cancers -- Results

- Empirically derived balance between precision (many samples) and homogeneity (smaller groups) -- 5 exposure groups:

  0.12 uT (n=347)

  0.21 uT (n=0.511)

  0.39 uT (n=821)

  0.62 uT (n=529)

  1.27 uT (n=634)
- Variation in exposure by company
- Many uncaptured influences on exposure

Occupational Magnetic Fields and Adult Cancers -- Results

Exposure (uT-yr)	Leukemia RR	Brain RR
0-<0.6	(1.00)	(1.00)
0.6-<1.2	1.04	1.61
1.2-<2.0	1.13	1.47
2.0-<4.3	0.95	1.65
>4.3	1.11	2.29
RR per uT-yr	1.01	1.07

Drinking Water Disinfection By-Products (DBPs) & Pregnancy

- Chlorination of drinking water needed to protect from infectious disease
- Generates chemical by-products due to reactions with organic matter in source water
- Exposure determined by water source and treatment method (geography), location in water distribution system, and water use behaviors – ingestion, bathing, swimming

Drinking Water DBPs & Pregnancy – Site Selection

- Site selection to optimize exposure distribution
- Required sufficiently large populations to allow recruitment of adequate numbers of participants early in pregnancy
- Identified three locations with distinctive water characteristics
  - Moderate chlorinated DBPs (low bromide in source water) – Raleigh, NC
  - Moderate brominated DBPs (high bromide in source water) – Galveston, TX
  - Low DBPs (water from deep wells) – Memphis, TN

Drinking Water DBPs & Pregnancy – Site Selection, cont.

- Minimize within-system variability (complex to model changes due to transit times)
- Free chlorine results in continued DBP formation in distribution system, spatial variation in exposure within service area
- Moderate chlorinated and brominated DBP site chosen for use of combined chlorine as terminal disinfectant
- Experimental verification that a single sampling point reflected system-wide levels of DBPs

Drinking Water DBPs & Pregnancy – Sampling & Analysis

- Sampled weekly from convenient location at moderate DBP sites, bi-weekly at low DBP site
- During annual flushing with free chlorine, sampled at multiple sites and generated average for system
- Primary analysis based on prior evidence: trihalomethanes (THM4), bromodichloromethane (BDCM), haloacetic acids (HAA9), total organic halide (TOX)

Drinking Water DBPs & Pregnancy -- Mean DBPs by Site (ppb)

	Cl site	Br site	Low DBP
THM4	63.3	60.5	4.2
Chloroform	45.6	11.9	---
BDCM	13.8	19.6	1.5
THM-Br	17.8	48.5	3.9
HAA9	43.2	45.7	3.5
TOX	172	186	16.5

Drinking Water DBPs & Pregnancy– Exposure Indices

- Concentration: measurement of weekly or biweekly water samples for each area
- Ingested amount: incorporate amount of water consumed, hot & cold, filtered and unfiltered
- Absorbed THMs from bathing/showering: incorporate duration and frequency of bathing
- Integrated THM exposure: ingested amount + bathing/showering contribution

Drinking Water DBPs & Pregnancy– Impact of Filter Use

- Faucet and pitcher filters used frequently(12-30% across study sites)
- Experimental work with popular devices to assess DBP removal efficiency
- THMs – complete removal by faucet filters, average of 40% removal by pitcher filters
- HAAs – 8-91% removal by faucet filters, 13-65% by pitcher filters
- TOX – 74% removal by faucet filters, 41% by pitcher filters

Drinking Water DBPs & Pregnancy– Impact of Heating

- Boiling removed essentially all THMs
- HAAs reduced by 75% on average
- TOX reduced by 30-40% with variation across study site due to varying constituents across sites

Drinking Water DBPs & Pregnancy– Ingested Amount

- Self-report of cup or glass size, number per day of hot and cold tap water or beverages prepared from tap water
- Reported use of filter at home and work (always, sometimes, rarely, never)
- Reported changes incorporated into time-specific estimate
- Calculation: ounces per day of water of hot and cold, filtered (faucet, pitcher) and unfiltered

Drinking Water DBPs & Pregnancy–Absorbed Dose

- Frequency and duration of bathing and showering combined with DBP concentration
- Estimated THM uptake factors from experiments used to calculate inhalation and dermal absorption from bathing and showering
- Estimated THM uptake from ingestion
- Indices: uptake from bathing/showering, total exposure including ingestion (µg/day)

Drinking Water DBPs & Pregnancy–Results

	DBP Index	
	Concentration (µg/L)	Ingested amount (µg)
Q1	(1.0)	(1.0)
Q2	1.7	0.8
Q3	1.1	1.0
Q4	0.9	0.9
Q5	0.8	1.0

Drinking Water DBPs & Pregnancy – Key Limitations

- No information on ambient THM levels from water use in homes
- Inherent limitations in the quality of self-reported information on water use
- Did not incorporate exposure from swimming despite contribution
- Challenge of isolating DBP exposure from community-level patterns of pregnancy loss related to ethnicity and other factors

Recommended Strategy I

- Develop understanding of process resulting in human exposure
  - Source of agent(s)
  - Distribution
  - Factors affecting exposure – environmental, behavioral
  - Confer with technical experts, those with first-hand experience, observe, experiment

Recommended Strategy II

- Seek setting that favors accurate exposure assignment
  - Wide range of exposure levels
  - Minimal within-group vs. between-group variability
  - Maximize “capturable” sources of exposure, minimize “noise”

Recommended Strategy III

- Address historical changes
  - Recognize limitations in present-day measurements
  - Understand how and why it has changed to model changes over time
  - Consider sampling or simulating past conditions (e.g., reconfigure job tasks, old technology)
  - Vary assumptions for sensitivity analysis

Recommended Strategy IV

- Determine data availability
  - Breadth, quality, representativeness of existing measurements
  - Need to integrate with knowledge of exposure sources and pathways
- Consider need/opportunity for original data collection
  - Area measurements, personal measurements, biomarkers
  - Comprehensive or for validation

Recommended Strategy V

- Determine optimal grouping of exposure using knowledge, measurements
  - Aggregations of job title
  - Distance from environmental sources
  - Tradeoff of homogeneity & precision
- Assign individual exposure using range of available information
  - Group data + individual behaviors/modifiers

Recommended Strategy VI

- Sensitivity analyses
  - Vary assumptions to assess impact on exposure assignment, relationship to health outcomes, determine where more work is needed
- Validation studies
  - More definitive assessment for subset
  - Validate routine assignment
  - Formal adjustment for measurement error

Themes in Exposure Assessment

- Multidisciplinary approach -- versatile
- Mix of common sense and technology
- First-hand knowledge of exposure sources, data quality
- Reconcile scientific goals with logistical constraints, make wise tradeoffs
- Recognize limitations and seek improvements