



## PHW250B Week 8 Reader

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# Cross-sectional studies

PHW250 F - Jack Colford

JACK COLFORD: In this lecture, I'm going to discuss cross-sectional studies with you.

## Outline

- Definition
- Purpose
- Sampling techniques
- Strengths & weaknesses
- Cross-sectional cohort design

First to talk about how cross-sectional studies are defined, and that is specifically how they're different from other studies. What their purpose is. How we sample populations in order to enroll participants in the cross-sectional study. What are the strengths and weaknesses of this design. And what is the very particular design that we refer to as the cross-sectional cohort design. That's a different flavor that we'll talk about a little bit.

## Definition of a cross-sectional study

- Study in which an investigator samples a target population to generate a "snapshot" of exposure and disease at that time.
  - Often uses sampling procedures so that the study population is representative of the target population.
  - Can also be used to reconstruct a cohort without doing a cohort study
  - Example: U.S. Census, Demographic and Health Surveys

First, let's define a cross-sectional study. Here, we as an investigator or other investigators, want to target some population just to get a snapshot of exposure and disease, both at the same time. And when we say same time that might be defined as a short period, like a month or a week or a year, but it's some defined period of time when we're taking a snapshot of the population.

In order to take this snapshot, we have to sample the population, so we use sampling procedures to ensure that the sample we have is representative of the target population. We can also use this approach to reconstruct a cohort without doing a cohort study. And examples of data sources where we might do cross-sectional studies are common ones, such as the US census or the international demographic and health surveys-- the DHS surveys.

## Purpose

- Can be used to generate hypotheses
- Can be used to estimate prevalence, perhaps to plan for a future study with a different design
- Can assess many exposures and outcomes at one time

Cross-sectional studies can be used to generate hypotheses. They can be used to estimate prevalence of exposures and diseases. And they are very valuable in planning for future studies that might involve a different design, because cross-sectional studies can be carried out so easily and quickly sometimes that they can serve as the foundation for building a future more complicated cohort study or trial. And another strength or part of their appeal is that they can assess many exposures and outcomes at one time.

## Sampling techniques

- Often the goal is for the study population to be representative of the target population.
- Some sub-populations may need to be excluded
  - E.g., for cost reasons for hard to reach populations
- Types of probability sampling
  - Random sampling
  - Cluster sampling
  - Stratified sampling
  - Probability proportionate to size sampling
  - (There are many other kinds and entire classes on this subject)



As I mentioned, when investigators conduct a cross-sectional study, it's necessary to sample the population of interest. And usually, we are very intent on making our sample of the population be representative of the target or larger population that we're trying to study. Now, we may have to exclude some sub-populations within our larger populations if we can't reach them. For example, if there are very hard to reach populations, we may not be able to include them in our sampling plan.

There are different types of sampling techniques, and in particular, sampling techniques called probability sampling. And several of these are called random sampling, clustered sampling, stratified sampling, and probability proportionate to size sampling. I'll go through each of these. And there are many other kinds of sampling techniques, and, in fact, entire classes here at Berkeley on this subject.

## Process of sampling

Random sampling	Cluster sampling	Stratified sampling
<ul style="list-style-type: none"><li>Define a sampling frame - often a list of <u>individuals</u> of an area or particular population. Could also be a map.</li><li>Randomly select <u>people</u> in the sampling frame to invite to participate in the study</li><li>Ensures study population is representative of target population</li></ul>	<ul style="list-style-type: none"><li>Define a sampling frame with <u>clusters of individuals</u> (e.g., households, neighborhoods, clinics)</li><li>Randomly select <u>clusters</u> in the sampling frame to invite to participate in the study</li><li>Can help reduce cost</li><li>Is often appropriate for studies of infectious diseases</li></ul>	<ul style="list-style-type: none"><li>Divide sampling frame into strata (e.g., age categories)</li><li>Randomly select <u>individuals within each stratum</u> to invite to participate in the study</li><li>Ensures that the study population includes people in all important categories</li><li>Analysis must use weights to account for stratified sampling</li></ul>



Three very commonly used approaches to sampling a population are random sampling, cluster sampling, and stratified sampling. Let's talk about each one and by way of being able to compare them. In a random sampling scheme, we're going to define a sampling frame. That's usually some list of individuals in a population or an area. This could also be a map or some other guide to the population that we're going to use from which to sample.

Then with some random process, we're going to select people who are in this frame and invite them to participate in the study. We usually can't afford to study everybody who's in the sampling frame, so we want to pick a sample from the sampling frame and make sure that our sample is representative of the entire sampling frame. And this ensures that the study population is representative of the target population itself.

I just want to emphasize this concept about the sampling frame. That this is the sort of tool or the mechanism by which we've enumerated the population. So it might be a list, it might be a registry, it might be a census, et cetera.

With cluster sampling, we first define a sampling frame that has clusters of individuals. And by clusters, I mean groupings like households, or neighbors, or clinics. Then, rather than randomly selecting individuals, we are first randomly selecting clusters in the sampling frame to invite people to participate in the study.

As you may imagine, this can help reduce cost a lot, because once I sample a cluster

of them, I have a whole group of people there that I'm going to approach. I don't go find them initially as individuals. I find clusters and then I try to get as many people from the cluster as my study design wants me to do. And this is often appropriate for studies of infectious and other diseases, but very commonly used in studies of infectious diseases.

Another type of sampling is called stratified sampling. And here we divide the sampling frame into strata-- plural of the word stratum. One example of this might be we might divide the population into age categories. Then within each of the individual stratum, we invite people to participate in the study who have been randomly selected.

This random selection is an important point, because we want to make sure that each selection from each stratum is representative of that stratum. This ensures that the study population includes people in all the important categories. And then the analysis subsequently has to use weighting to account for the fact that we stratified the sampling.

## Population proportionate to size (PPS) sampling

- A type of sampling in which the probability of a cluster being selected is proportional to the size of the cluster and a pre-set number of people per cluster are enrolled.
- In the first stage, larger clusters have bigger probability of being sampled
- In the second stage, since the same number of individuals per cluster are enrolled, individuals in large clusters have a lower probability of being sampled
- As a result, each individual in the population has the same probability of being sampled
- Useful when cluster size varies substantially because it ensures that people in large clusters are equally as likely to be enrolled as people in small clusters (and vice versa)



Finally, an important type of sampling in cross-sectional studies is population proportionate to size sampling, or abbreviated as PPS. When PPS sampling, the probability of a cluster being selected is proportional to the size of its cluster and a pre-set number of people per cluster are enrolled. In other words, a cluster that's four times as large as another cluster has a four time higher chance of being included as a cluster in the study. Doesn't mean it will definitely be included, but its probability of being selected is higher by that amount.

In the first stage of PPS sampling, larger clusters have this bigger probability of being sampled, as I explained. And then there's a second stage when the same number of individuals per cluster are enrolled, therefore individuals in a large cluster have a lower probability of being sampled. Think of it this way, if I have one cluster that's 1,000 people and one cluster that's 200 people, and if I'm picking 10 people from all clusters, in the cluster with 1,000 people my chance of being one of those 10 is much lower than it is if I'm in the cluster with 200 people.

As a result, each individual in the population end up having the same probability of being sampled across the entire cluster. Every one in the 1,000 person cluster has the same probability of being sampled-- one in 1,000. And everybody in the 200 person sample cluster has a one in 200 chance of being sampled. This is useful when cluster size vary substantially, because it ensures that people in large clusters are equally likely to be enrolled as people in small clusters and vice versa.

## Strengths & weaknesses

### Strengths

- Relatively inexpensive and quick
- Efficient method of calculating prevalence
- Study population representative of target population

### Weaknesses

- It is difficult to be certain whether exposure preceded disease
- Recall of past disease may be subject to recall bias
- Length-biased sampling

Let's talk about some of the strengths and weaknesses of the cross-sectional study design. Its strengths include the fact that this design is relatively inexpensive and quick compared to other designs. It's a very efficient way to calculate prevalence, because we're randomly sampling from the population. And it generates a study population that's representative of the larger target population we hope we're representing and then studying.

But there are weaknesses to cross-sectional design. It can be difficult to be certain whether the exposure preceded the disease. And this is one of the key weaknesses of the cross-sectional design. We don't know that when we measure-- let's say smoking and lung cancer in a cross-sectional study-- we don't know whether someone began smoking before the lung cancer occurred or whether they might have started smoking after the lung cancer occurred. That reversal of timing there is something we can't sort out in a cross-sectional study usually.

Another weakness in a cross-sectional study is that the recall of past disease may be subject to recall bias. The memory of the past exposure or disease may be subject to recall bias. And finally, a weakness of a cross-sectional design is the potential for length-biased sampling as we've discussed before.

## Cross-sectional cohort design

- Reconstruct a hypothetical cohort using a cross-sectional design
- Can help reduce concerns about temporality
  - **Example:** study of whether attention-deficit hyperactivity disorder (ADHD) in childhood is a risk factor for major depressive disorder
  - Interview participants aged 13-50 years at one point in calendar time
  - Administer a survey to assess current depression symptoms
  - Administer a survey to assess past ADHD
- Relies on participants' recall to reconstruct it

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Hudson et al., 2005

Let's talk about another type of cross-sectional study called a cross-sectional cohort design. Here, we reconstruct a hypothetical cohort using a cross-sectional design. And this is to help us reduce concerns about temporality. For example, let's say we're studying attention deficit hyperactivity disorder in childhood as a possible risk factor for subsequent major depressive disorder.

In this study, we might interview participants aged 13 to 50 years of age at one point in calendar time. That's the cross-sectional measure now at this point in calendar time. We give them a survey to assess what their current depression symptoms are right now. But we're interested in whether or not prior ADHD led to the current depression now. We administer a survey to assess their past ADHD by asking them, did you have ADHD in the past?

We've used the participants recall about past exposure-- ADHD-- to reconstruct and build a cohort here. The early thing we're looking for was the presence of ADHD. We gathered that by giving a questionnaire to people. But we measure them currently in a cross-sectional way their current depression symptoms.

## Summary of key points

- Cross-sectional studies can be used to generate hypotheses and validly estimate prevalence.
- They can assess many exposures and outcomes at one time.
- It can be difficult to establish the time ordering of exposure and outcome in cross-sectional studies.
- Cross-sectional studies can be subject to length-biased sampling.

To summarize the key points for a cross-sectional study-- this design can be used to generate hypotheses and validly estimate prevalence. It can be used to assess many exposures and outcomes at one time-- that's a particular advantage. But it can be difficult to establish the time ordering of exposure and outcome in cross-sectional studies. And finally, cross-sectional studies can be subject to the length-biased sampling that we've discussed previously.

Lecture: Evaluating and Reporting Cross Sectional Studies



## Evaluating and reporting cross-sectional studies

PHW250 F - Jack Colford

JACK COLFORD: Let's discuss a systematic way to evaluate and report cross-sectional studies.

# Assessment of cross-sectional studies

## Were potential confounding factors sought and controlled for in the analysis?

- Did the investigators anticipate and gather information on potential confounding factors?
- What method(s) were used to assess and control for confounding?

## What steps were taken to minimise bias?

- Was the outcome clear, specific, and measurable?
- Was an appropriate measure of disease used?
- Was the exposure clear, specific, and measurable?
- Are there any concerns about misclassification of the exposure or outcome?
- Is the study population representative of the target population?
- Was time ordering of exposure and outcome taken into consideration in the study design?

When we assess cross-sectional studies, couple of thoughts to keep in mind, couple of ideas to keep in mind are, first, were there potential confounding factors sought and controlled for in the analysis? So this is quite similar to what we've done previously in cohort studies and case control studies.

But as before, the question here is, did the investigators anticipate and gather information on any potential confounding factors? And then what did they do to assess and control for these confounding factors? Did they do multivariate analysis? Or did they use matching? Or exactly what did they do to identify and adjust for the confounders?

So how about minimizing bias in cross-sectional studies? Were the investigators using clear, specific, and measurable outcomes? By clear, specific, and measurable, we mean in the eyes of the reader. Was there an appropriate measure of disease used? Was the exposures that they were measuring clear, specific, and measurable? Do you have any concerns about whether they misclassified any of the exposures or the outcomes? And if so, was that misclassification non-differential or differential?

Was the study population representative of the target population? Remember how when we do a cross-sectional study, we hope that the sample that we picked to represent the larger population from which we are picking is a representative sample. So if the overall population is 30% female, then the sample should be something close to 30% female. And on whatever measure, there should be a random representative sample of the whole population.

And then finally, was any time ordering of exposure and outcome taken into consideration in the study design? We talked about the cross-sectional cohort design as one way to do this before. But was there any time ordering about the data that were collected?

## STROBE Checklist for reporting case-control studies



- The checklist arose out of concerns that observational studies were poorly and inconsistently reported.
- Poor reporting makes it difficult to assess strengths and weaknesses of a study.
- A group of methodologists, researchers, and editors developed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations to improve the quality of reporting of observational studies.
- 22 item checklist
- 18 items are common to cohort studies, case-control studies and cross-sectional studies.
- 4 items are specific to each of the three study designs.

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So once again, we see our friend the STROBE checklist that's used for observational studies. And as before, just a reminder, this is the Strengthening and Reporting of Observational Studies in Epidemiology, or STROBE, recommendations to improve the quality of reporting. It's a 22-item checklist. 18 are common to all the observational studies. Four are specific for each of the three different observational study designs we've talked about-- cohort studies, case control studies, and now, here, cross-sectional studies.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable



I'm not going to repeat the key elements that are found in the STROBE statement. But you see them here in the next set of slides. And it's just a good checklist for you to go through when you're reading a cross-sectional study to help organize your thinking about the things that were collected.

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	<ul style="list-style-type: none"> <li>(a) Describe all statistical methods, including those used to control for confounding</li> <li>(b) Describe any methods used to examine subgroups and interactions</li> <li>(c) Explain how missing data were addressed</li> <li>(d) If applicable, describe analytical methods taking account of sampling strategy</li> <li>(e) Describe any sensitivity analyses</li> </ul>



We won't do too much more about statistical methods in analyzing cross-sectional data. But here's a set of five questions you can ask in the Statistical Methods section.

What were the methods that were used to report the data? How did they control for confounding? Were there subgroups and interactions studied? Were missing data addressed? What was the sampling strategy in finding the sample that was used? And if a sampling strategy was used, how was that worked into the analytic strategy in coming up with the results? And were there any sensitivity analyses done?

<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  (b) Give reasons for non-participation at each stage  (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders  (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included  (b) Report category boundaries when continuous variables were categorized  (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

With respect to the main results, I just want to highlight, again, this issue of adjusting for confounders. And are the authors being very specific about what methods were used to adjust for confounding? And how did they arrive at confidence intervals for their adjusted estimates?

<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based



And finally, once again, in Discussion, I want to highlight the Limitations section. What do the authors tell us about what they see as limitations of their cross-sectional design? Might be that their sample wasn't representative of the overall population. Might be the overall population isn't somehow the right overall population from which to be sampling.

Were there any sources of bias? Selection bias or information bias, as we've discussed many times before. How did they deal with that? And as before, did they identify clearly any sources of funding and how that might lead to conflicts of interest?

## Summary of key points

- We recommend that you use the STROBE reporting checklist when publishing results of a cross-sectional study.
- The article by Vandenbrouke et al. 2007 article provides detailed examples of how to use the STROBE checklist with an example paper.

So in summary, once again, suggestion to use the STROBE checklist when you're looking through the results of a published cross-sectional study. Take a look at the Vandenbrouke article from 2007 that we provided you, giving detailed examples of how to use the STROBE checklist with an example paper.

## STROBE Checklist for Cross-sectional Studies

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p>
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	<p>(a) Give the eligibility criteria, and the sources and methods of selection of participants</p>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) If applicable, describe analytical methods taking account of sampling strategy</p> <p>(e) Describe any sensitivity analyses</p>
<b>Results</b>		
Participants	13*	<p>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(c) Consider use of a flow diagram</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p>
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

Lecture: Case Study - Iraq Mortality Study



## Case study: Iraq mortality study

PHW250 B – Andrew Mertens



This video will present a case study of a cross-sectional study that estimated deaths attributable to the Iraq war. I'll note that this is an emotionally difficult topic to discuss, especially in a dispassionate, academic epidemiology perspective, but it provides an important case study in the use of cross-sectional studies for challenging-to-research epidemiologic questions.



## The Iraq War

- 2001: “9/11” attacks in the U.S.
- 2003: U.S. invasion of Iraq
- 2006: execution of Saddam Hussein
- 2010: Last U.S. combat force left Iraq



### Violent vs nonviolent events

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Szklo 2nd ed, Fig 1-6B

To briefly give an overview of the Iraq war, in 2001 there were the well-known 9/11 attacks in the United States. And two years later, in 2003, the US invaded Iraq. In 2006 was the execution of Saddam Hussein. And in 2010, the last US combat force left Iraq. It was a very violent war. The study that we're going to talk about in this video intended to estimate the number of deaths and the \*proportion of deaths attributable to violent versus non-violent events from 2002 to 2006.

## The health risks of living in a war zone

- • Violence
- • Insufficient water supplies
- • Non-functional sewerage
- • Restricted electricity supply
- • Deterioration in health services
- • Loss of health providers



Berkeley School of  
Burnham et al., 2006

What are the health risks of living in a war zone? \*Well, obviously violence is a primary potential risk. But also, there's lots of other potential causes of morbidity and mortality. \*Water supplies can be interrupted, making it difficult to maintain good hygiene and to drink water that's safe. \*The sewer system can be disrupted or nonfunctional, which can lead to the spread of fecal-oral transmitted diseases. \*The electricity supply can be restricted or cut off, which can prevent people from staying at safe temperatures or getting the kind of medical care that they need, from keeping their food refrigerated. \*Health services can deteriorate and \*often many physicians and other types of health providers will leave the country or may pass away during the war.

## How do you count deaths in a war setting?

- • Hospital death data
- • Mortuary tallies
- • Media reports
- • Household surveys



**None are perfect**

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Burnham et al., 2006

How do you count deaths in a war setting? Well, there's several different approaches and none of them are perfect. We can use data from hospitals that keep track of the number of deaths. But of course, there are lots of deaths that occur outside of hospitals and the people who end up in a hospital may be systematically different from people who don't. So this isn't, on its own, a great way to accurately estimate the number of deaths. Mortuaries have similar drawbacks. So we can count the number of people who show up there, and again, the kind of people who show up there may be systematically different from those who do not. For example, people who pass away in very rural areas maybe less likely to show up in a mortuary tally. Media reports will sometimes have death counts but these may be based on anecdotal information and are likely not to be as scientific as other potential sources of information. And then the focus of this video here is household surveys. So we're going to talk about that in quite a bit of detail.

## The Lancet study

- • Second of two studies on this topic published in *The Lancet*
- • National household survey in 2006 to measure deaths between 2002 and 2006
- • Received wide media coverage
- • Faced criticisms from some journalists, epidemiologists, statisticians, and government officials (but was supported by others in these professions)

Articles

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**Mortality after the 2003 invasion of Iraq: a cross-sectional cluster sample survey**

Gilbert Burnham, Riyad Laffa, Shannon Doocy, Les Roberts

**Summary**  
**Background** An excess mortality of nearly 100 000 deaths was reported in Iraq for the period March, 2003–September, 2004, attributed to the invasion of Iraq. Our aim was to update this estimate.

**Methods** Between May and July, 2006, we did a national cross-sectional cluster sample survey of mortality in Iraq. 50 clusters were randomly selected from 16 Governorates, with every cluster consisting of 40 households. Information on deaths from these households was gathered.

**Findings** Three misattributed clusters were excluded from the final analysis; data from 1849 households that contained 12 801 individuals in 47 clusters was gathered. 1474 births and 629 deaths were reported during the observation period. Pre-invasion mortality rates were 5·5 per 1000 people per year (95% CI 4·3–7·1), compared with 13·3 per 1000 people per year (10·9–16·1) in the 40 months post-invasion. We estimate that as of July, 2006, there have been 654 965 (392 979–942 636) excess Iraqi deaths as a consequence of the war, which corresponds to 2·5% of the population in the study area. Of post-invasion deaths, 601 027 (426 369–793 663) were due to violence, the most common cause being gunfire.

**Interpretation** The number of people dying in Iraq has continued to escalate. The proportion of deaths ascribed to coalition forces has diminished in 2006, although the actual numbers have increased every year. Gunfire remains the most common cause of death, although deaths from car bombing have increased.

Published online October 12, 2006  
DOI:10.1016/S0140-6736(06)64491-9  
See Comment page 1395  
Johns Hopkins Bloomberg School of Public Health,  
Baltimore, MD 21205, USA  
(Prof G Burnham MD,  
S Doocy PhD, L Roberts PhD),  
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There were two well publicized studies in The Lancet that came out on this topic by the same group of investigators. \*We're focusing on the second of these two studies in this video. \*This was a national household survey that was conducted in 2006 to measure deaths that occurred between 2002 and 2006. \*And this article received a wide amount of media coverage, both positive and negative. \*It received criticisms from a variety of types of people, so journalists, epidemiologists, statisticians, government officials from different countries. But there were also many people who supported the merits of the study and believed its findings. This is a nice example of a cross-sectional study that gained a lot of attention and was trying to do something quite important. Oftentimes in epidemiology, we think of cross-sectional studies as sort of less desirable than a case control or trial or cohort study. But this study kind of highlights how impactful cross-sectional studies can be and that in this particular setting, this really is the only kind of study that could be done to answer this research question.

## Questions to consider:

- What kind of sampling would you use for a cross-sectional survey of this research question?
- What challenges might investigators face in implementing this study in a wartime setting?
- How would you measure excess deaths due to war? What information would you need?
- What would you want to know about the study's methods to believe its findings?



Before we go on, take a minute to review these questions and jot down on a piece of paper what your initial response is.\* So the first question is, what kind of sampling would you use for a cross-sectional survey of this research question? And again, the purpose of the study was to estimate the number of deaths that occurred during the beginning of the Iraq war. In a previous video, we introduced you to different kinds of sampling. We talked about random sampling, cluster sampling, stratified sampling, and probability proportionate to size sampling. So think about those and which one you would choose for a cross-sectional survey of this research question.

\*Next, take a minute to think about what challenges you think the investigators might face in implementing this study because it was conducted during war times. How might this affect the way they designed the study, the types of questions they ask, who they employ to implement the survey, et cetera.

\*Another question, how would you measure excess deaths due to war? So these are deaths above and beyond deaths that you would expect in a non-wartime setting. What information would you need to measure these excess deaths?

\*And finally, what would you want to know about the study's methods and design in order to believe its findings? So we get to the end of the study and I've already told you that the findings were controversial. As someone reading the article, what would you want to know to decide whether you would believe the findings? Take a moment

## Sampling methods

- • Identified streets and blocks and assigned them numbers
- • Cluster-based sampling - enrolled households in clusters close to each other
- • Sampling conducted in three stages:
  - • **First stage:** 50 clusters were selected systematically by Governorate with a population proportional to size approach
  - • **Second stage:** administrative units within Governorates were listed by population or estimated population, and location(s) were selected randomly proportionate to population size
  - • **Third stage:**
    - Randomly selected main street from a list
    - Randomly selected residential street crossing main street from a list
    - Randomly select a house on the residential street and survey this house and the nearest 40 households

Here are the sampling methods used by Burnham et al. in this study. \*They collected map information from different regions of Iraq and identified streets and blocks and assigned them numbers. \*And then they performed cluster-based sampling. The clusters were defined as groups of households that were close to each other.

\*And they conducted sampling in three stages. \*In the first stage, they chose 50 clusters systematically within governorates, which are essentially regions. And they used a population proportional to size approach. They don't state this in the article directly, but presumably their choice of PPS sampling was because of the variation in population size of the different clusters within each governorate.

\*In the second stage, they chose administrative units within governorate, so it's a sub region, essentially. They listed each of these administrative units by a population or their estimated population. And then they randomly selected locations, again with PPS sampling. Once they'd gotten down to these smaller administrative units, \*they began the third stage of sampling. So within that stage, they went back to their map. They randomly selected a main street from their numbered list of streets. And then again, they randomly selected a cross street of the main street.

And then on that residential street, they randomly selected a house and started the survey at that house and then completed the survey in the nearest 40 households that consented. In order to complete the sampling, they needed a few pieces of information. So they needed a map. They also needed estimated population within administrative units within governance. You can imagine that in a wartime setting, it might be difficult to rely on any

information they may have gathered prior to the study, since houses may be bombed, people may be entering and exiting population in unexpected ways.

So the population size likely wasn't perfectly accurate or consistent with the information they used during the sampling process.

## Statistical methods

2002 - 2006

- • **Mortality rates** were calculated over the period of recall using the mid-interval population **Recall bias?**
  - The standard errors for mortality rates accounted for the clustered sampling method
- • **Excess deaths** = 
$$\frac{(\text{post-war mortality rates}) - (\text{predicted pre-war mortality rates})}{\text{x 2004 mid-year population size}}$$
- • In this case, the investigators did not have pre-war data, so they predicted those data using a statistical model that was fit with data from the post-war period.

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Burnham et al., 2006

Here's their statistical methods. They calculated \*mortality rates over the period of recall that was from \*2002 to 2006. And they used the mid interval population for the denominator. So that was in 2004, was the middle of that interval. So they tallied up all of the deaths from 2002 to 2006 and divided that by the population in 2004. And they calculated standard errors that accounted for their clustered sampling method.

One thing to point out here is that they're relying on recall over a four year period where there's a lot of tumult. And so of course, we have to wonder, to what extent their data was subject to \*recall bias.

\*They also calculated excess deaths. And these again are the excess deaths that they are attributing to war. To do this, they first calculated \*the post-war mortality rates, which is really the during war mortality rates from 2003 to 2006. And they also calculated something called \*the predicted pre-war mortality rates.

What is a predicted rate? Well, \*in this case, they didn't have the information from before the Iraq war. They may have had a little information from 2002, right before the invasion, but not a substantial period of time. And they likely didn't ask respondents to recall prior to the start of 2002 because it would have just been such a long recall period and that would be really unusual to try to ask people to remember that far back.

So what they had to do was use the data they had that was primarily from the war period and used a statistical model to try to estimate what the pre-war mortality rates were. And they fit the model with data from the pre and post-war period. But as you may recall, their

recall period was from 2002 to 2006, so most of their data was from the post-war period

## Results: mortality rates

	Period				Mortality rates for total time post-invasion	p value*
	Pre-invasion	Mar 03–Apr 04	May 04–May 05	June 05–June 06		
Crude mortality rate	5.5 (4.3–7.1)	7.5 (5.8–9.7)	10.9 (8.1–14.0)	19.8 (14.6–26.7)	13.2 (10.9–16.1)	<0.0001
Non-violent mortality rate	5.4 (4.1–6.8)	4.5 (3.2–5.8)	5.0 (3.8–6.3)	6.9 (5.1–9.5)	6.0 (4.8–7.5)	0.523
Violent mortality rate	0.1 (0.0–0.4)	3.2 (1.8–4.9)	6.6 (4.0–9.8)	12.0 (7.2–16.8)	7.2 (5.2–9.5)	<0.0001
Excess mortality rate	0	2.6 (0.6–4.7)	5.6 (2.7–8.6)	14.2 (8.6–21.5)	7.8 (4.7–11.2)	NA

Data are number of deaths per 1000 people per year (95% CI). \*Post-invasion mortality rate vs pre-invasion mortality rate.

Table 3: Mortality rates by time

Here are the mortality rates that they estimated. \*Let's just focus on the first row of the table, the crude mortality rate. They estimated that \*pre-invasion there were 5.5 deaths per 1,000 people per year. \*And then in the next few columns are the year-specific mortality rates, 7.5, 10.9, and 19.8. \*And then they also averaged over those three years for the total post-invasion rate, which was 13.2. \*They also estimated nonviolent versus violent mortality rates. This is based on respondents' report for the cause of death. \*The violent mortality rate was a little higher than the non-violent mortality rate but the confidence intervals overlapped quite a bit. So it's not possible to statistically distinguish between these two rates. \*And then the excess mortality rate is basically the difference between the post and pre-war periods. And that was estimated to be 7.8 on average. 7.8 deaths per 1,000 people per year on average.

## Results: excess deaths

### Previous estimates:

- Iraq Body Count estimate:  
43491 to 48283 Iraqis were killed since the invasion up to 2006.
- Iraqi Ministry of the Interior estimates were 75% higher than those of the Iraq Body Count
- An Iraqi non-governmental organisation, Iraqiyun, estimated 128,000 deaths from the time of the invasion until 2005

Now let's go over the excess death findings. First, I'll review the previous estimates prior to the study. So there were several different sources of information that estimated the number of deaths during the Iraq war. \*There was something called the Iraq body count estimate. They estimated around 43,000 to 48,000 Iraqis were killed since the invasion and all the way up until 2006. So this is following the same time period as the study that we're talking about in this video. \*The Iraqi Ministry of Interior had estimated a number 75% higher than the 43,000 to 48,000 estimate. \*And then there was another Iraqi non-governmental organization that estimated 128,000 deaths from invasion until 2005. So that's one year less than we're thinking about here and a much larger number than in this first bullet point. OK, let's compare these previous estimates to what Burnham et al. reported.

# Results: excess deaths

## Previous estimates:

- Iraq Body Count estimate: 43491 to 48283 Iraqis were killed since the invasion up to 2006.
- Iraqi Ministry of the Interior estimates were 75% higher than those of the Iraq Body Count
- An Iraqi non-governmental organisation, Iraqiyun, estimated 128,000 deaths from the time of the invasion until 2005

## Burnham et al.'s estimates:

- Between 2003 and 2006, an additional 654 965 (392 979–942 636) Iraqis died above what would have been expected on the basis of the pre-invasion crude mortality rate as a consequence of the coalition invasion
- 601 027 (426 369–793 663) deaths due to violence
- About 2.5% of the population in the study area died

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Burnham et al., 2006

So they took those mortality rates from the previous slide and used that to predict the total number of deaths. \*And they estimated that between 2003 and 2006 there were an additional 654,965 Iraqi deaths above what would have been expected on the basis of the pre invasion crude mortality rate. So again, these are the excess deaths. 654,000 is a much, much larger number than any of the numbers on the left hand side of the slide. \*And they estimated that a little over 600,000 of those deaths were due to violence and \*that 2.5% of the population in the study area had died. It's worth pausing to take a look at their 95% confidence intervals in the parentheses. \*So for that first number, 654,000, the confidence interval ranges pretty wide from 392,000 to 942,000. So it's a wide interval but the interval is still-- the bottom of the interval is still quite far from any of the other previous estimates on the left hand side of the slide.\* So this was a substantially higher estimated number of excess deaths.

## Limitations reported by Burnham et al.

- • Bias in sampling due to extreme limitations in sampling process due to safety concerns
  - Restrictions on number of surveyors, length of survey, collection of identifiers
  - No revisits to households possible
- • Under-reporting to be expected, particularly for infant deaths
- • Over-reporting possible, although surveyors did confirm deaths with death certificates (92%)
- • Survivor bias when entire households were killed
- • Population data used in cluster sampling were at least 2 years old
  - Large scale migration occurred during the period and migration could be associated with death of household members, introducing bias
- • No clusters were enrolled in two areas due to miscommunication

Before we talk about the response to this article, let's go over some of the limitations that they reported themselves. \*In the article, they note the extreme limitations that they faced in the sampling process due to safety concerns. They had restrictions on the number of people they could hire to conduct surveys, how long the survey could be, which directly affects how many questions they could ask. And they weren't able to collect any identifying information which would have been helpful if they needed to, for example, go back to visit a household later to confirm information. They weren't able to do many visits anyway because of safety concerns.

\*And they expected the deaths would be under reported, particularly for infants, due to their cultural understanding of the area in a wartime setting.

\*But also they say that over reporting could have been possible and they did their best to evaluate whether this was true or whether it occurred. They asked for death certificates when available. And they were able to confirm 92% of the deaths reported by respondents with death certificates. So if we believe what's on the death certificates, that suggests that their data is quite good.

\*Now, there's still other forms of bias that the study could be subject to, for example, survivor bias, when an entire household is killed, it doesn't end up in the survey. It may still be part of the denominator from the previous census information that was used for sampling but there's no one present in order to report the deaths that would go in the numerator. So this can lead to underreporting.

\*Their sampling process relied on population data that was at least two years old. And this is probably because they couldn't-- there wasn't anything that was newer that was available to them. And it's quite likely that there was large scale migration during the period of the study and that migration should be associated with death of household numbers introducing bias. So it's hard to say which direction that would go in but you could see how, perhaps, if many people in your household died, you'd be more likely to try to leave the area.

\*And then also there were two areas that they intended to include in the study, but they didn't end up enrolling them due to miscommunication. So this was another limitation.

## Media coverage and response

- "It is an estimate and not a precise count, and researchers acknowledged a margin of error that ranged from 426,369 to 793,663 deaths."
- The study "surveyed 1,849 Iraqi families in 47 different neighborhoods across Iraq. The selection of geographical areas in 18 regions across Iraq was based on population size, not on the level of violence, they said."

### *Iraqi Dead May Total 600,000, Study Says*

By SABRINA TAVERNISE and DONALD G. McNEIL, Jr. OCT. 11, 2006



A boy at his father's coffin in Baghdad yesterday. Death rates were higher outside the capital, the study said.  
Khalid Mohammed/Associated Press

BAGHDAD, Oct. 10 — A team of American and Iraqi public health researchers has estimated that 600,000 civilians have died in violence across **Iraq** since the 2003 American invasion, the highest estimate ever for the toll of the war here.

<https://www.nytimes.com/2006/10/11/world/middleeast/11casualties.html>

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Here's a snapshot of a New York Times article that discussed the study. And this was one of many different articles that reported these large numbers. \*The New York Times article said it is an estimate and not a precise count. And researchers acknowledged a margin of error that ranged from 426,000 to 793,000 deaths. So it's a nice example of a reporter interpreting a confidence interval when reporting on an epidemiologic study. \*And in the next bullet point, here's a quote that talks about the sampling methods used in this article. So it says the study surveyed 1,849 Iraqi families in 47 neighborhoods across Iraq. The selection of geographical areas in 18 regions across Iraq was based on population size, not on the level of violence, they said. So that gets back to our PPS sampling.

## Media coverage and response

- "The study comes at a sensitive time for the Iraqi government, which is under pressure from American officials to take action against militias driving the sectarian killings."
- "The American military has disputed the Iraqi figures, saying that they are far higher than the actual number of deaths from the insurgency and sectarian violence, in part because they include natural deaths and deaths from ordinary crime, like domestic violence."

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Here's some more quotes from the article. \*It says, the study comes at a sensitive time for the Iraqi government, which is under pressure from American officials to take action against militias driving the actual number of deaths from the insurgency and sectarian killings. \*And then in the next bullet point it goes on to say that the American military has disputed the Iraqi figures. So this just goes to show that this was a very sensitive article. There were a lot of different stakeholders at play who were hoping for smaller numbers of deaths. And as a result, this article in *The Lancet* received a lot of scrutiny and a lot of attention, much more so than a typical epidemiologic study would.

## Media coverage and response

- “Statistics experts in the United States who were able to review the study said the methods used by the interviewers looked legitimate.”
- One expert “said interviewing urban dwellers chosen at random was “the best of what you can expect in a war zone” but that “the number of deaths in the families interviewed [...] was too few to extrapolate up to more than 600,000 deaths across the country.”
- Donald Berry, chairman of biostatistics at M. D. Anderson Cancer Center in Houston, was even more troubled by the study, which he said had “a tone of accuracy that’s just inappropriate.”

### *Iraqi Dead May Total 600,000, Study Says*

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Here's a few more quotes. \*So statistics experts in the United States who were able to review the study said the methods used by the interviewers looked legitimate.

\*One expert said interviewing urban dwellers chosen at random was the best of what you can expect in a war zone, but that the number of deaths in the families interviewed was too few to extrapolate up to more than 600,000 deaths across the country. This is essentially saying that they needed a larger and more representative sample in order to produce national estimates from the data in their survey. Another way of saying that is that this expert had concerns about the external validity of this cross-sectional survey.

\*And then there's a final quote from another expert in biostatistics that said he was troubled by the study which had a tone of accuracy that's just inappropriate. So that's a way of saying that the sort of level of confidence the authors had in their estimates was too high, given all the limitations they faced, even though the effort was solid, there's still some major limitations that could affect the interpretations of the findings here.

## Criticisms of the study

- Pre-war estimates not reliable
- Use of local interviewers could introduce bias since they may have opposed to the occupation
- Other surveys conducted later produced lower estimates
- Investigators did not disclose the questionnaire, data entry form, and other study instruments in detail

\*Other criticisms of the study included that the pre-war estimates were not reliable.

\*They used local interviewers, which could introduce bias since many of them were opposed to the occupation and may want to sort of show that there were a large number of deaths associated with occupation.

\*There were other surveys conducted later on that produced lower estimates.

\*And some people criticized the investigators for not disclosing the questionnaire, data entry forms, and their other study instruments in detail.

And this gets to an issue of transparency in research that we're going to cover later in this course sequence. Back at that time it was relatively unusual to disclose all of these different kinds of documents for an important study like this. But because of recent scandals in different scientific fields that have found that it's very difficult to reproduce estimates in different studies, more and more authors are starting to automatically disclose this information at the time of publication so that readers can fully vet the findings themselves.

## Summary of key points

- • This study illustrates the use of a cross-sectional design to estimate rates based on participant recall
- • This is essentially a cross-sectional cohort design because it tried to re-construct the cohort's experience from 2002-2006.
- • Epidemiologic studies in war-time settings face unique threats to validity.
- • While some of the criticisms of the study are valid (including limitations listed by the authors themselves), in this type of setting, it's very difficult to conduct an epidemiologic with ideal methods.



To summarize, \*the study illustrates the use of a cross sectional study design to estimate mortality rates that are fully based on a participant recall.

\*And it's essentially a cross-sectional cohort design because what the authors were trying to do was recreate the experience of the cohort in Iraq from 2002 to 2006 in the year 2006.

\*The study highlights how epidemiologic studies in wartime settings face unique threats to validity.

\*And while many of the criticisms of the study are valid and the authors themselves listed many of these limitations, in this particular, challenging, setting, it's difficult to come up with a study design that would have been more appropriate for this question than this particular design

## Mortality after the 2003 invasion of Iraq: a cross-sectional cluster sample survey



Gilbert Burnham, Riyad Lafta, Shannon Doocy, Les Roberts

### Summary

**Background** An excess mortality of nearly 100 000 deaths was reported in Iraq for the period March, 2003–September, 2004, attributed to the invasion of Iraq. Our aim was to update this estimate.

*Lancet* 2006; 368: 1421–28

**Methods** Between May and July, 2006, we did a national cross-sectional cluster sample survey of mortality in Iraq. 50 clusters were randomly selected from 16 Governorates, with every cluster consisting of 40 households. Information on deaths from these households was gathered.

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See *Comment* page 1395

**Findings** Three misattributed clusters were excluded from the final analysis; data from 1849 households that contained 12 801 individuals in 47 clusters was gathered. 1474 births and 629 deaths were reported during the observation period. Pre-invasion mortality rates were 5.5 per 1000 people per year (95% CI 4.3–7.1), compared with 13.3 per 1000 people per year (10.9–16.1) in the 40 months post-invasion. We estimate that as of July, 2006, there have been 654 965 (392 979–942 636) excess Iraqi deaths as a consequence of the war, which corresponds to 2.5% of the population in the study area. Of post-invasion deaths, 601 027 (426 369–793 663) were due to violence, the most common cause being gunfire.

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**Interpretation** The number of people dying in Iraq has continued to escalate. The proportion of deaths ascribed to coalition forces has diminished in 2006, although the actual numbers have increased every year. Gunfire remains the most common cause of death, although deaths from car bombing have increased.

### Introduction

There has been widespread concern over the scale of Iraqi deaths after the invasion by the US-led coalition in March, 2003. Various methods have been used to count violent deaths, including hospital death data from the Ministry of Health, mortuary tallies, and media reports.<sup>1,2</sup> The best known is the Iraq Body Count, which estimated that, up to September 26, 2006, between 43 491 and 48 283 Iraqis have been killed since the invasion.<sup>1</sup> Estimates from the Iraqi Ministry of the Interior were 75% higher than those based on the Iraq Body Count from the same period.<sup>2</sup> An Iraqi non-governmental organisation, Iraqiyun, estimated 128 000 deaths from the time of the invasion until July, 2005, by use of various sources, including household interviews.<sup>3</sup>

professionals adds further risks. People displaced by the on-going sectarian violence add to the number of vulnerable individuals. In many conflicts, these indirect causes have accounted for most civilian deaths.<sup>11,12</sup>

In 2004, we did a survey of 33 randomly selected clusters of 30 households with a mean of eight residents throughout Iraq to determine the excess mortality during the 17.8 months after the 2003 invasion.<sup>8</sup> The survey estimated excess mortality of at least 98 000 (95% CI 8000–194 000) after excluding, as an outlier, the high mortality reported in the Falluja cluster. Over half of excess deaths recorded in the 2004 study were from violent causes, and about half of the violent deaths occurred in Falluja.

To determine how on-going events in Iraq have affected mortality rates subsequently, we repeated a national household survey between May and July, 2006. We measured deaths from January, 2002, to July, 2006, which included the period of the 2004 survey.

### Methods

#### Participants and procedures

To measure mortality we did a national cross-sectional cohort study of deaths from January, 2002, through July, 2006. Household information was gathered about deaths that occurred between January 1, 2002, and the invasion of March 18, 2003, in all households and these data were compared with deaths that occurred from the time of the invasion through to the date of survey. A sample size of 12 000 was calculated to be adequate to identify a doubling of an estimated pre-invasion crude mortality

The US Department of Defence keeps some records of Iraqi deaths, despite initially denying that they did.<sup>4</sup> Recently, Iraqi casualty data from the Multi-National Corps-Iraq (MNC-I) Significant Activities database were released.<sup>5</sup> These data estimated the civilian casualty rate at 117 deaths per day between May, 2005, and June, 2006, on the basis of deaths that occurred in events to which the coalition responded. There also have been several surveys that assessed the burden of conflict on the population.<sup>6–8</sup> These surveys have predictably produced substantially higher estimates than the passive surveillance reports.

Aside from violence, insufficient water supplies, non-functional sewerage, and restricted electricity supply also create health hazards.<sup>9,10</sup> A deteriorating health service with insecure access, and the flight of health

rate of 5·0 per 1000 people per year with 95% confidence and a power of 80%, and was chosen to balance the need for robust data with the level of risk acceptable to field teams. Sampling followed the same approach used in 2004,<sup>8</sup> except that selection of survey sites was by random numbers applied to streets or blocks rather than with global positioning units (GPS), since surveyors felt that being seen with a GPS unit could put their lives at risk. The use of GPS units might be seen as targeting an area for air strikes, or that the unit was in reality a remote detonation control. By confining the survey to a cluster of houses close to one another it was felt the benign purpose of the survey would spread quickly by word of mouth among households, thus lessening risk to interviewers.

As a first stage of sampling, 50 clusters were selected systematically by Governorate with a population proportional to size approach, on the basis of the 2004 UNDP/Iraqi Ministry of Planning population estimates (table 1). At the second stage of sampling, the Governorate's constituent administrative units were listed by population or estimated population, and location(s) were selected randomly proportionate to population size. The third stage consisted of random selection of a main street within the administrative unit from a list of all main streets. A residential street was then randomly selected from a list of residential streets crossing the main street. On the residential street, houses were numbered and a start household was randomly selected. From this start household, the team proceeded to the adjacent residence until 40 households were surveyed. For this study, a household was defined as a unit that ate together, and had a separate entrance from the street or a separate apartment entrance.

The two survey teams each consisted of two female and two male interviewers, with the field manager (RL) serving as supervisor. All were medical doctors with previous survey and community medicine experience and were fluent in English and Arabic. A 2-day training session was held. Decisions on sampling sites were made by the field manager. The interview team were given the responsibility and authority to change to an alternate location if they perceived the level of insecurity or risk to be unacceptable. In every cluster, the numbers of households where no-one was at home or where participation was refused were recorded. In every cluster, queries were made about any household that had been present during the survey period that had ceased to exist because all members had died or left. Empty houses or those that refused to participate were passed over until 40 households had been interviewed in all locations.

The survey purpose was explained to the head of household or spouse, and oral consent was obtained. Participants were assured that no unique identifiers would be gathered. No incentives were provided. The survey listed current household members by sex, and asked who had lived in this household on January 1, 2002. The interviewers then asked about births, deaths, and in-migration and out-migration, and confirmed that the reported inflow and exit of residents explained the differences in composition between the start and end of the recall period. Separation of combatant from non-combatant deaths during interviews was not attempted, since such information would probably be concealed by household informants, and to ask about this could put interviewers at risk. Deaths were recorded only if the decedent had lived in the household continuously for 3 months before the event. Additional probing was done to establish the cause and circumstances of deaths to the extent feasible, taking into account family sensitivities. At the conclusion of household interviews where deaths were reported, surveyors requested to see a copy of any death certificate and its presence was recorded. Where differences between the household account and the cause mentioned on the certificate existed, further discussions were sometimes needed to establish the primary cause of death.

The study received ethical approval from the Committee on Human Research of the Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, and the School of Medicine, Al Mustansiriya University, Baghdad, Iraq.

### Statistical analysis

Data entry and analysis was done with Microsoft Excel, SPSS version 12.0, and STATA version 8. Period mortality rates were calculated on the basis of the mid-interval population and with regression models. Mortality rates and relative risks of mortality were estimated with log-linear regression models in STATA.<sup>13</sup> To estimate the relative risk, we used a model that allowed for a baseline

	Mid-year 2004 population	Number of clusters
Baghdad	6 554 126	12
Ninewa	2 554 270	5
Basrah	1 797 758	3
Sulamaniyah	1 715 585	3
Thi-Qar	1 493 781	3
Babylon	1 472 405	3
Erbil	1 418 455	3
Diyala	1 392 093	3
Anbar	1 328 776	3
Salah al-Din	1 119 369	2
Najaf	978 400	2
Wassit	971 280	1
Qadissiya	911 640	1
Tameem	854 470	1
Missan	787 072	1
Kerbala	762 872	1
Muthanna	554 994	0
Dahuk	472 238	0
Total	27 139 584	47

Table 1: Province populations and cluster allocation

	Children (0–14 years)		Adults (15–59 years)		Elderly people (60+ years)	All deaths by cause†
	Men	Women				
<b>Pre-invasion (n=82)</b>						
Non-violent deaths	14 (100%)	19 (95%)	6 (100%)	40 (96%)	80 (98%)	
Heart disease/stroke	0	6 (30%)	2 (33%)	12 (29%)	20 (24%)	
Cancer	1 (7%)	5 (25%)	1 (17%)	8 (20%)	15 (18%)	
Chronic illness	1 (7%)	5 (25%)	0	9 (22%)	15 (18%)	
Infant	11 (79%)	NA	NA	NA	11 (13%)	
Accident	0	3 (15%)	2 (33%)	2 (5%)	7 (9%)	
Old age	NA	NA	NA	8 (20%)	8 (10%)	
Infectious disease	0	0	0	1 (2%)	1 (1%)	
Other (non-violent)	1 (7%)	0	1 (17%)	0	3 (4%)	
Violent deaths	0	1 (5%)	0	1 (2%)	2 (2%)	
Other explosion/ordnance	0	1 (5%)	0	0	1 (1%)	
Air strike	0	0	0	1 (2%)	1 (1%)	
Total deaths	14 (100%)	20 (100%)	6 (100%)	41 (100%)	82 (100%)	
<b>Post-invasion (n=547)</b>						
Non-violent deaths	40 (60%)	37 (14%)	39 (72%)	126 (92%)	247 (46%)	
Heart disease/stroke	1 (2%)	15 (6%)	11 (20%)	74 (54%)	102 (19%)	
Cancer	1 (2%)	5 (2%)	14 (26%)	11 (8%)	33 (6%)	
Chronic illness	0	5 (2%)	3 (6%)	18 (13%)	28 (5%)	
Infant	29 (43%)	NA	NA	NA	29 (5%)	
Accident	8 (12%)	5 (2%)	6 (11%)	4 (3%)	23 (4%)	
Old age	NA	NA	NA	19 (14%)	19 (4%)	
Infectious disease	1 (2%)	1 (0%)	1 (2%)	0	3 (1%)	
Other (non-violent)	0	6 (2%)	4 (7%)	0	10 (2%)	
Violent deaths	26 (39%)	235 (86%)	15 (28%)	11 (8%)	300 (55%)	
Gunshot	3 (5%)	142 (49%)	6 (11%)	9 (7%)	169 (31%)	
Other explosion/ordnance	4 (6%)	33 (12%)	2 (4%)	1 (1%)	42 (8%)	
Air strike	13 (20%)	23 (9%)	2 (4%)	1 (1%)	39 (7%)	
Car bomb	3 (5%)	28 (10%)	5 (9%)	0	38 (7%)	
Unknown (violent)	1 (2%)	5 (2%)	0	0	6 (1%)	
Accident	2 (3%)	4 (1%)	0	0	6 (1%)	
Total deaths	66 (100%)	272 (100%)	54 (100%)	137 (100%)	547 (100%)	

Data are number (% of deaths within age group). NA=not applicable. \*Age was reported for 610 of 629 deaths that occurred; sex reporting was complete. †Includes deaths with unknown age. Causes of death were much the same between the sexes both pre-invasion and post-invasion for children ( $p=0.342$  pre-invasion and  $p=0.189$  post-invasion) and elderly individuals ( $p=0.215$  pre-invasion and  $p=0.483$  post-invasion). Causes of death were much the same by sex in adults pre-invasion ( $p=0.297$ ), but significantly different post-invasion ( $p<0.0001$ ).

Table 2: Pre-invasion and post-invasion deaths by age and cause (n=629)\*

rate of mortality and a distinct relative rate for three 14-month intervals post-invasion—March, 2003–April, 2004, May, 2004–May, 2005, and June, 2005–June, 2006. The SE for mortality rates were calculated with robust variance estimation that took into account the correlation between rates of death within the same cluster over time.<sup>14</sup> The log-linear regression model assumed that the variation in mortality rates across clusters is proportional to the average mortality rate; to assess the effect of this assumption we also obtained non-parametric CIs by use of bootstrapping.<sup>13,15</sup> As an additional sensitivity analysis, we assessed the effect of differences across clusters by extending models to allow the baseline mortality rate to vary by cluster. We estimated the numbers of excess

deaths (attributable rates) by subtraction of the predicted values for the pre-war mortality rates from the post-war mortality rates in the three post-invasion periods. Mortality projections with model rates were applied to 2004 mid-year population estimates for Iraq, minus the population of Dahuk and Muthanna, which were not sampled, to ascertain mortality projections.<sup>9</sup>

#### Role of the funding source

Massachusetts Institute of Technology, which was the major funder, had no role in the collection or the analysis of the data, or the preparation of the publication. The Johns Hopkins Center for Refugee and Disaster Response used some general funds to cover research expense. All

authors had full access to all the data; the corresponding author had final responsibility to submit for publication.

## Results

The survey was done between May 20 and July 10, 2006. Only 47 of the sought 50 clusters were included in this analysis. On two occasions, miscommunication resulted in clusters not being visited in Muthanna and Dahuk, and instead being included in other Governorates. In Wassit, insecurity caused the team to choose the next nearest population area, in accordance with the study protocol. Later it was discovered that this second site was actually across the boundary in Baghdad Governorate. These three misattributed clusters were therefore excluded, leaving a final sample of 1849 households in 47 randomly selected clusters. In 16 (0.9%) dwellings,

residents were absent; 15 (0.8%) households refused to participate. In the few apartment houses visited, the team progressed to the nearest households within the building. One team could typically complete a cluster of 40 households in 1 day. No interviewers died or were injured during the survey.

Households where all members were dead or had gone away were reported in only one cluster in Ninewa and these deaths are not included in this report. The 1849 households that completed the survey had 12 801 household members at the time of the survey; thus, the mean household size was 6.9 people. Of the 12 529 residents whose sex was recorded, 6123 (48.9%) were male. The study population at the beginning of the recall period (January 1, 2002) was calculated to be 11 956, and a total of 1474 births and 629 deaths were reported during the study period; age was reported for 610 of 629 deaths, sex reporting was complete. During the survey period there were 129 households (7%) that reported in-migration, and 152 households (8%) reported out-migration. Survey teams asked for death certificates in 545 (87%) reported deaths and these were present in 501 cases. The pattern of deaths in households without death certificates was no different from those with certificates.

Of the 629 deaths reported, 547 (87%) were in the post-invasion period (March, 2003, to June, 2006) compared with 82 (13%) in the pre-invasion period (January, 2002, to March, 2003; table 2). Most deaths (n=485; 77%) were in males, and this was true for both periods, but more pronounced in the pre-invasion period (57 of 82 deaths pre-invasion vs 428 of 547 deaths post-invasion). The male-to-female ratio of post-invasion deaths was 3.4 for all deaths, and 9.8 for violent deaths (all deaths: 144 female, 485 male; violent death: 28 female, 274 male). In general, deaths by age group followed the expected J-shaped demographic curve; however, by contrast, most deaths in males were in the middle age groups (figure 1).

The crude mortality rate in the pre-invasion period was 5.5 per 1000 people per year (95% CI 4.3–7.1) and for the overall post-invasion period was 13.3 per 1000 people per year (10.9–16.1; table 3). A four-fold increase in the crude mortality rate was recorded during the study period, with a high of 19.8 per 1000 people per year

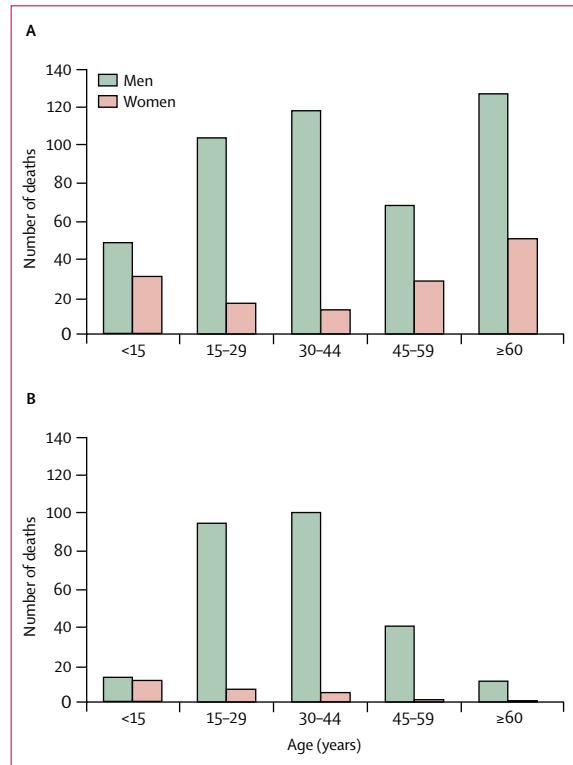


Figure 1: Deaths where age and sex known since start of study period  
(A) All deaths (n=610). (B) Violent deaths (n=287).

	Period				Mortality rates for total time post-invasion	p value*
	Pre-invasion	Mar 03–Apr 04	May 04–May 05	June 05–June 06		
Crude mortality rate	5.5 (4.3–7.1)	7.5 (5.8–9.7)	10.9 (8.1–14.0)	19.8 (14.6–26.7)	13.2 (10.9–16.1)	<0.0001
Non-violent mortality rate	5.4 (4.1–6.8)	4.5 (3.2–5.8)	5.0 (3.8–6.3)	6.9 (5.1–9.5)	6.0 (4.8–7.5)	0.523
Violent mortality rate	0.1 (0.0–0.4)	3.2 (1.8–4.9)	6.6 (4.0–9.8)	12.0 (7.2–16.8)	7.2 (5.2–9.5)	<0.0001
Excess mortality rate	0	2.6 (0.6–4.7)	5.6 (2.7–8.6)	14.2 (8.6–21.5)	7.8 (4.7–11.2)	NA

Data are number of deaths per 1000 people per year (95% CI). \*Post-invasion mortality rate vs pre-invasion mortality rate.

Table 3: Mortality rates by time

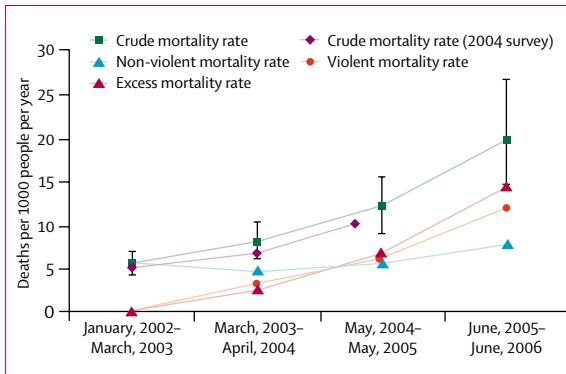


Figure 2: Mortality rates, 2002-06

(14.6–26.7) between June, 2005, and June, 2006 (figure 2 and table 3).

Post-invasion excess mortality rates showed much the same escalating trend, rising from 2.6 per 1000 people per year (0.6–4.7) above the baseline rate in 2003 to 14.2 per 1000 people per year (8.6–21.5) in 2006 (figure 2 and table 3). Excess mortality is attributed mainly to an increase in the violent death rate; however, an increase in the non-violent death rate was noted in the later part of the post-invasion period (2005–06). The post-invasion non-violent excess mortality rate was 0.7 per 1000 people per year (−1.2 to 3.0).

Of the 302 conflict-related violent deaths reported, 300 (99%) were post-invasion (table 4). An increase in violent death rates was seen in the post-invasion period (figure 2). Analysis for trend showed that this rate for violent deaths increased significantly in every period after the invasion ( $p<0.0001$ ) compared with the pre-invasion period.

Of the 302 violent deaths, 274 (91%) were of men, and within this group, deaths concentrated in the 15–29 and 30–44 year old age groups (figure 1). Most violent deaths

were due to gunshots (56%); air strikes, car bombs, and other explosions/ordnance each accounted for 13–14% of violent deaths. The number of deaths from gunshots increased consistently over the post-invasion period, and a sharp increase in deaths from car bombs was noted in 2006.

Violent deaths that were directly attributed to coalition forces or to air strikes were classified as coalition violent deaths. In many other cases the responsible party was not known, or the households were hesitant to specifically identify them. Deaths attributable to the coalition accounted for 31% (95% CI 26–37) of post-invasion violent deaths. The proportion of violent deaths attributable to the coalition was much the same across periods ( $p=0.058$ ). However, the actual number of violent deaths, including those that resulted from coalition forces, increased every year after the invasion. Deaths in men of military age, defined as 15–44 years of age, were disproportionately high and accounted for 59% (52–65) of post-invasion violent deaths, despite this subgroup accounting for only 24.4% of the Iraqi population.<sup>16</sup> No difference in the proportion of violent deaths in men of military age was noted between deaths attributed to the coalition or other/unknown sources ( $p=0.168$ ). Mortality rates by Governorate are shown in figure 3.

Of the 327 non-violent deaths that were reported, 80 (24%) occurred pre-invasion and 247 (76%) occurred post-invasion (table 2). Non-violent mortality rates before and after invasion are shown in table 3. The mortality rates from non-violent causes were essentially unchanged until the first 6 months of 2006, at which point they increased by almost two deaths per 1000 people per year; however, this increase was not significant.

The male-to-female ratio of non-violent deaths was 1.8 (211 male vs 116 female deaths;  $p<0.0001$ ). 17% of non-violent deaths occurred in those aged under 15 years,

	Period				Total
	Pre-invasion	March 03–April 04	May 04–May 05	June 05–June 06	
Risk of death	..	1.5 (1.1–2.0)	2.2 (1.5–3.4)	3.6 (2.3–5.6)	..
Cause of violent death					
Coalition	1 (50%)	16 (36%)	35 (39%)	43 (26%)	95 (31%)
Other	0	4 (9%)	17 (19%)	50 (30%)	71 (24%)
Unknown	1 (50%)	25 (56%)	38 (42%)	72 (44%)	136 (45%)
Specific cause of violent death					
Gunshot	0	36 (80%)	46 (51%)	87 (53%)	169 (56%)
Car bomb	0	1 (2%)	7 (8%)	30 (18%)	38 (13%)
Other explosion/ordnance	1 (50%)	1 (2%)	21 (23%)	20 (12%)	43 (14%)
Air strike	1 (50%)	6 (13%)	13 (14%)	20 (12%)	40 (13%)
Unknown	0	0	2 (2%)	4 (2%)	6 (2%)
Accident	0	1 (2%)	1 (1%)	4 (2%)	6 (2%)
Total deaths	2 (100%)	45 (100%)	90 (100%)	165 (100%)	302 (100%)

Data are risk ratio (95% CI) or number (% of total deaths in specific period).

Table 4: Violent deaths by cause and time

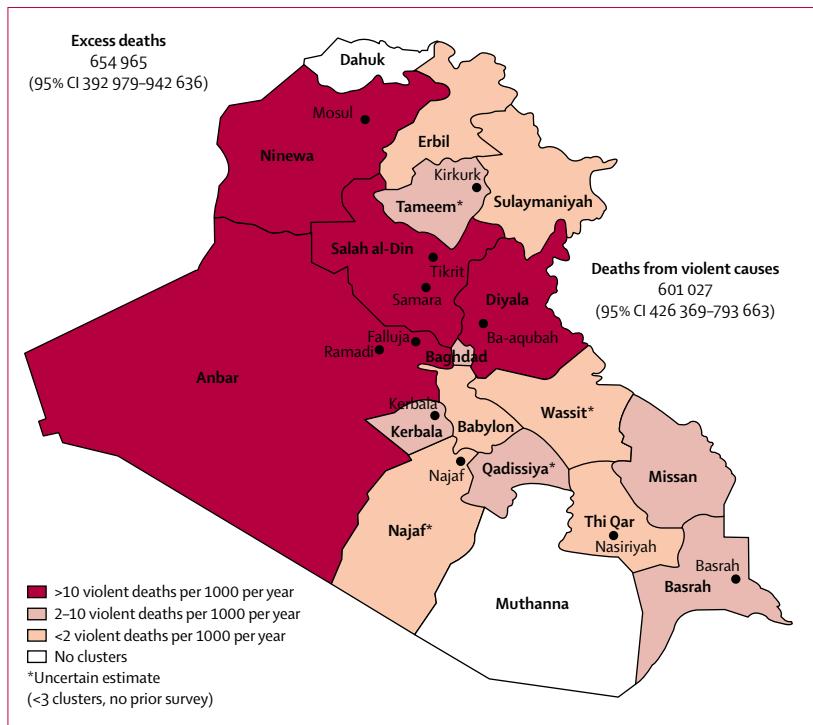


Figure 3: Death rates due to violent causes per Governorate

Mortality rates in Governorates with fewer than three clusters were confirmed with 2004 survey data; estimates for provinces with fewer than three clusters that could not be confirmed are potentially uncertain due to the small sample size.

32% in 15–59 year olds, and 52% in those over 60 years. Non-violent deaths by time, age, and cause are described in table 2. Cardiovascular conditions were the main cause of non-violent death and accounted for 37% of non-violent deaths over the entire study period. Other notable sources of non-violent mortality included cancer (14%), chronic illnesses (13%), infant deaths (12%), accidents (11%), and old age (8%). Causes of non-violent deaths were much the same both pre-invasion and post-invasion ( $p=0.290$ ).

We estimate that between March 18, 2003, and June, 2006, an additional 654 965 (392 979–942 636) Iraqis have died above what would have been expected on the basis of the pre-invasion crude mortality rate as a consequence of the coalition invasion. Of these deaths, we estimate that 601 027 (426 369–793 663) were due to violence.

### Discussion

We estimate that, as a consequence of the coalition invasion of March 18, 2003, about 655 000 Iraqis have died above the number that would be expected in a non-conflict situation, which is equivalent to about 2.5% of the population in the study area. About 601 000 of these excess deaths were due to violent causes. Our estimate of the post-invasion crude mortality rate represents a doubling of the baseline mortality rate, which, by the Sphere standards, constitutes a humanitarian emergency.<sup>17</sup>

Our estimate of the pre-invasion crude or all-cause mortality rate is in close agreement with other sources.<sup>18,19</sup>

The post-invasion crude mortality rate increased significantly from pre-invasion figures, and showed a rising trend. The increasing number of violent deaths follows trends of bodies counted by mortuaries, as well as those reported in the media and by the Iraq Body Count.<sup>1,5,20</sup>

Application of the mortality rates reported here to the period of the 2004 survey<sup>8</sup> gives an estimate of 112 000 (69 000–155 000) excess deaths in Iraq in that period. Thus, the data presented here validates our 2004 study, which conservatively estimated an excess mortality of nearly 100 000 as of September, 2004.

Our estimate of excess deaths is far higher than those reported in Iraq through passive surveillance measures.<sup>1,5</sup> This discrepancy is not unexpected. Data from passive surveillance are rarely complete, even in stable circumstances, and are even less complete during conflict, when access is restricted and fatal events could be intentionally hidden. Aside from Bosnia,<sup>21</sup> we can find no conflict situation where passive surveillance recorded more than 20% of the deaths measured by population-based methods. In several outbreaks, disease and death recorded by facility-based methods underestimated events by a factor of ten or more when compared with population-based estimates.<sup>11,22–25</sup> Between 1960 and 1990, newspaper accounts of political deaths in Guatemala correctly reported over 50% of deaths in years of low violence but less than 5% in years of highest violence.<sup>26</sup> Nevertheless, surveillance tallies are important in monitoring trends over time and in the provision of individual data, and these data track closely with our own findings (figure 4).

Mortality rates from violent causes have increased every year post-invasion. By mid-year 2006, 91 violent deaths had occurred in 6 months, compared with 27 post-invasion in 2003 and 77 in 2004, and 105 for 2005, suggesting that violence has escalated substantially. The attributed cause of these deaths has also changed with time. Our data show that gunfire is the major cause of death in Iraq, accounting for about half of all violent deaths. Deaths from air strikes were less commonly reported in 2006 than in 2003–04, but deaths from car explosions have increased since late 2005. The proportion of violent deaths attributed to coalition forces might have peaked in 2004; however, the actual number of Iraqi deaths attributed to coalition forces increased steadily through 2005. Deaths were not classified as being due to coalition forces if households had any uncertainty about the responsible party; consequently, the number of deaths and the proportion of violent deaths attributable to coalition forces could be conservative estimates. Distinguishing criminal murders from anti-coalition force actions was not possible in this survey.

Across Iraq, deaths and injuries from violent causes were concentrated in adolescent to middle age men. Although some were probably combatants, a number of factors would expose this group to more risk—eg, life style, automobile travel, and employment outside the

home. The circumstances of a number of deaths from gunshots suggest assassinations or executions. Coalition forces have been reported as targeting all men of military age.<sup>27,28</sup>

From January, 2002, until the invasion in 2003, virtually all deaths in Iraq were from non-violent causes. The main causes of non-violent deaths were much the same as the leading causes of hospital deaths reported by the Ministry of Health in 2004 and 2005 (unpublished data). Death rates from non-violent causes remained essentially unchanged from pre-invasion levels until 2006, when they rose by 2·0 deaths per 1000 per year above the pre-invasion baseline, an increase that was not significant. We are unsure of the reason for the observed change in sex ratio of adults aged 15–59 years dying from non-violent causes between pre-invasion and post-invasion periods (table 2), or why deaths from cardiovascular causes rose after the invasion.

All surveys have potential for error and bias. The extreme insecurity during this survey could have introduced bias by restricting the size of teams, the number of supervisors, and the length of time that could be prudently spent in all locations, which in turn affected the size and nature of questionnaires. Further, calling back to households not available on the initial visit was felt to be too dangerous. Families, especially in households with combatants killed, could have hidden deaths. Under-reporting of infant deaths is a wide-spread concern in surveys of this type.<sup>29,30</sup> Entire households could have been killed, leading to a survivor bias. The population data used for cluster selection were at least 2 years old, and if populations subsequently migrated from areas of high mortality to those with low mortality, the sample might have over-represented the high-mortality areas. The miscommunication that resulted in no clusters being interviewed in Duhuk and Muthanna resulted in our assuming that no excess deaths occurred in those provinces (with 5% of the population), which probably resulted in an underestimate of total deaths. Families could have reported deaths that did not occur, although this seems unlikely, since most reported deaths could be corroborated with a certificate. However, certificates might not be issued for young children, and in some places death certificates had stopped being issued; our 92% confirmation rate was therefore deemed to be reasonable.

Large-scale migration out of Iraq could affect our death estimates by decreasing population size. Out-migration could introduce inaccuracies if such a process took place predominantly in households with either high or low violent death history. Internal population movement would be less likely to affect results appreciably. However, the number of individual households with in-migration was much the same as those with out-migration in our survey.

Although interviewers used a robust process for identifying clusters, the potential exists for interviewers to be drawn to especially affected houses through conscious or unconscious processes. Although evidence

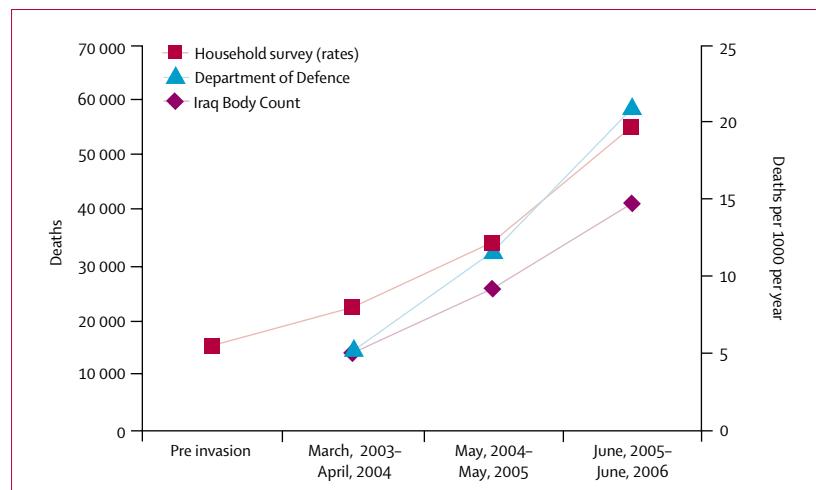


Figure 4: Trends in number of deaths reported by the Iraq Body Count and the MultiNational Corps-Iraq and the mortality rates found by this study

of this bias does not exist, its potential cannot be dismissed.<sup>31</sup> Furthermore, families might have misclassified information about the circumstances of death. Deaths could have been over or under-attributed to coalition forces on a consistent basis. The numbers of non-violent deaths were low, thus, estimation of trends with confidence was difficult. Not sampling two of the Governorates could have underestimated the total number of deaths, although these areas were generally known as low-violence Governorates. Finally, the sex of individuals who had died might not have been accurately reported by households. Female deaths could have been under-reported, or there might have been discomfort felt in reporting certain male deaths.

The striking similarity between the 2004 and 2006 estimates of pre-war mortality diminishes concerns about people's ability to recall deaths accurately over a 4-year period. Likewise, the similar patterns of mortality over time documented in our survey and by other sources corroborate our findings about the trends in mortality over time.<sup>1,5,32</sup>

In Iraq, as with other conflicts, civilians bear the consequences of warfare. In the Vietnam war, 3 million civilians died; in the Democratic Republic of the Congo, conflict has been responsible for 3·8 million deaths; and an estimated 200 000 of a total population of 800 000 died in conflict in East Timor.<sup>33–35</sup> Recent estimates are that 200 000 people have died in Darfur over the past 31 months.<sup>36</sup> We estimate that almost 655 000 people—2·5% of the population in the study area—have died in Iraq. Although such death rates might be common in times of war, the combination of a long duration and tens of millions of people affected has made this the deadliest international conflict of the 21st century, and should be of grave concern to everyone.

At the conclusion of our 2004 study<sup>8</sup> we urged that an independent body assess the excess mortality that we saw

in Iraq. This has not happened. We continue to believe that an independent international body to monitor compliance with the Geneva Conventions and other humanitarian standards in conflict is urgently needed. With reliable data, those voices that speak out for civilians trapped in conflict might be able to lessen the tragic human cost of future wars.

#### Contributors

G Burnham, as principal investigator, was involved in the study design and ethical approval, took part in the analysis and interpretation of results, and led the writing of the paper. R Lafta managed the field survey in Iraq, participated in the study design and the analysis, interpretation, and preparation of the manuscript. S Doocy managed the study data and was involved in the analysis, interpretation, and the writing of the manuscript. L Roberts instigated the study and assisted with the analysis and interpretation of the data and the writing of the manuscript.

#### Conflict of interest statement

We declare that we have no conflict of interest.

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Lecture: Ecological Studies



The logo for the Berkeley School of Public Health is displayed. It features the word "Berkeley" in a large, blue serif font. To the right of "Berkeley" is a blue circular icon with a white swirl pattern, followed by the text "School of Public Health" in a smaller, blue sans-serif font.

# Ecological studies

PHW250 F - Jack Colford

JACK COLFORD: Let's talk now about ecological studies.

## Outline

- Rationale for ecologic studies
- Levels of measurement
- Types of ecologic studies
  - Multiple group designs
  - Time trend designs
  - Mixed designs
  - Multilevel design
- Effect estimation
- Bias & confounding in ecologic studies



I'll organize my comments around the rationale for ecologic studies, the different levels of a measurement, which here refers to individual versus group level measurement, the types of ecologic studies, specifically multiple group designs, time trend designs, mixed designs, and multi-level designs, how we estimate effects in ecological studies since we do not have individual level data, and how ecologic studies control for confounding and try to avoid bias and what sort of biases exist in ecologic studies. A couple initial comments I'll make is you'll see the words ecological and ecologic used interchangeably, including within our presentations. This has nothing to do with the environment or ecology. This term ecologic refers to groups of individuals used in studies.

# Rationale for ecologic studies

- **Low cost and convenience**
  - Can be completed with existing data, such as registry and census data
- **Measurement limitations of individual-level studies**
  - In certain types of research (e.g., studies of air pollution) it is not very difficult to accurately measure exposure at the individual for many subjects
- **Design limitations of individual-level studies**
  - Individual level studies may not be practical for estimating exposure effects if the exposure varies very little in the study area
- **Interest in ecologic effects**
  - Ecologic effects are of interest when studying social processes or population interventions such as new policies
- **Simplicity of analysis and presentation**
  - In large, complex studies at the individual level, it may be simpler to perform ecologic analyses (e.g., data from National Health Interview Survey are often analyzed ecologically)

The rationale for ecologic studies is multifold. These are very low cost and convenience studies because they can be completed with existing data, such as you might have in registry and census data and you might be able to get these easily on your computer, do these on a very short frame. There are measurement limitations in individual level studies, for example, in certain types of research like studies of air pollution. It's very difficult to accurately measure exposure at the individual for many subjects. There are design limitations of individual level studies. Individual level studies may not be practical for estimating exposure effects if the exposure varies very little in the study area.

Sometimes our principal interest is actually in the ecologic effect that is the group level effect. So these effects were of interest when we're studying things such as social processes or population interventions and their effects from new policies. And finally, there can be some simplicity of analysis and presentation. When we look at large complex studies at the individual level it might be simpler to perform ecological analyzes, for example, data from the National Health Interview Survey are often analyzed ecologically, that is, at a group level.

## Levels of measurement in ecologic studies

**Aggregate measures:**  
summaries of observations derived from individuals in each group

Example: proportion of smokers



**Environmental measures:**  
physical characteristics of the place in which people live or work

Example: air pollution



**Global measures:**  
attributes of groups, organizations, places

Examples: population density, existence of a specific law, type of health care system



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There are various levels of measurement in ecologic studies. These are three levels we'll talk about are aggregate measures, environmental measures, and global measures. Aggregate measures are summaries of observations derived from individuals in each group. For example, what's the proportion of smokers in the population of this country? That's an aggregate measure. Environmental measures are sometimes used. These are physical characteristics of a place in which people live or work, for example, what's the air pollution level in the Bay Area? That's an environmental measure for a group or an area.

Finally, global measure, these are attributes of groups, organizations, or places. For example, population density or the existence of a specific law or specific regulation like a smoking regulation or a type of health care system. These are global measures that apply to the entire group, organization, place, et cetera.

## Multiple-group ecologic designs

- **Exploratory study**
  - Compare the rate of disease among many regions or populations during the same period
  - **Example:** Compare disease rates between migrants and their offspring and residents of their countries of emigration and immigration
- **Etiologic study**
  - Assess the ecologic association between the average exposure level and the rate of disease among many groups
  - Most common type of ecologic design; typically unit of analysis is geographic region
  - **Example:** examine association between gamma-radiation and the incidence of childhood cancers

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There are multiple group ecologic designs that are used. Two types we'll talk about are the exploratory study where we look at the rates of disease among many regions or populations during the same period to kind of explore how do these areas differ one from another with respect to their rates of disease.

And then are there things about these areas that are different, one from the other, that might be linked to that difference in rate of disease. For example, if smoking is very different in different populations or subgroups of populations, do we see differences in health status in these different groups? An example also might be comparing disease rates between migrants and their offspring and residents of their countries of emigration or immigration. Another type of multiple group ecologic design is the etiologic study. In this type of design, we assess the ecological association between the average exposure level and the rate of disease among many groups.

This is the most common type of ecologic design and the typical unit of analysis here is a geographic region. For example, if we compare the association between gamma radiation and the incidence of childhood cancer among different groups, this is a typical etiologic-type study with an ecologic design.

## Time trend ecologic designs

- **Exploratory study**
  - Compare the rate of disease over time in one geographically defined population
  - Time series data can be used to forecast future rates and trends (common in social sciences)
  - **Example:** Compare disease rates in a country before and after a new vaccine is introduced
- **Etiologic study**
  - Assess the ecologic association between change in average exposure level and change in disease rate in one geographically defined population
  - **Example:** examine associations between average exposure to radiation, which changes over time, and the incidence of childhood leukemia

There are time trend types of ecologic designs used both for exploration and for etiologic studies. If we compare the rates of disease over time in one geographically-defined population, that's an exploratory study. We could use time series data to forecast future rates and trends.

We've seen a trend in the past and we project that into the future. This is commonly used in social sciences. For example, let's compare disease rates in a country before and after a new vaccine is introduced. This is an exploratory type ecologic study using a time trend. An etiologic example of a time trend ecologic study might be to examine associations between average exposure to radiation, which changes over time, and the incidence of childhood leukemia. The goal here is to assess the ecologic association between change in the average exposure level and change in disease rate in one geographically defined population.

Think about that. We're trying to look at changes in two averages. Changes in the average exposure and change in the disease rate itself.

## Causal inference in time trend ecologic designs

- Causal inference for both types is complicated.
  - Changes in disease classification and diagnostic criteria can introduce confounding in observed rates of disease.
    - E.g., introduction of a new molecular test for a disease may greatly increase the detection rate for an infectious disease
  - Analysis must account for the induction/latent period between first exposure to a risk factor and disease detection.

Let's talk a little bit about causal inference in time trend ecologic designs. This is a complicated topic. Here, we're thinking about changes in disease classification and diagnostic criteria that can introduce confounding and observe rates of disease. For example, if a new molecular test is introduced into a population, it might greatly increase the detection rate for an infectious disease. This is not some biologic process that's going on, but this is a function of something that's been introduced in the population that is changing the trend of what's happening because of the increased diagnosis.

Any analysis has to account for the induction or latent period between the first exposure to a risk factor and disease detection. And that can change because of the introduction of the new test.

## Mixed ecologic designs

- **Exploratory study**
  - Combine basic features of the exploratory multi-group study and the exploratory time trend study
  - **Example:** examine changes in sunlight exposure during youth and melanoma mortality stratifying by region
- **Etiologic study**
  - Assess the ecologic association between the average exposure level and the rate of disease among many groups
  - Can compare changes over time within groups and differences among groups
  - **Example:** examine whether hard drinking water is protective of cardiovascular disease by comparing changes in CVD mortality in multiple towns with water-hardness changes in those towns

There are another group of ecologic designs called mixed ecologic designs. And these can also be exploratory or etiologic. The exploratory type of this study would be to combine the basic features of a multi group study and the exploratory time trend. An example might be changing sunlight exposure during youth and melanoma mortality when we stratify by region. As sunlight exposure changes as youth grow, what happens to melanoma mortality when we look in different regions?

And an etiologic example here might be to assess the ecologic association between the average exposure level and the rate of disease among many groups. Here we can compare changes over time within groups and differences among groups. An example, let's look at whether hard drinking water is protective for cardiovascular disease by changing cardiovascular disease mortality in multiple towns with water hardness changes in those towns from the Rothman examples. We look at how water hardness change over time in these towns and then we look at how cardiovascular disease mortality changed over time.

## Multi-level ecologic designs

- One solution to the problem of separating individual and contextual effects is to incorporate both individual and ecologic measures in the same analysis
- E.g., include each subject's individual exposure level as well as an average exposure level for all members of a group
- This clarifies the sources and magnitude of ecologic and cross-level bias
- It allows us to separate biologic, contextual, and ecologic effects
- Particularly useful in social epidemiology, infectious disease epidemiology, and evaluation of population level interventions

One solution to the problem of separating individual and contextual effects, that is, these kind of group level effects, is to incorporate both individual and ecologic measures in the same analysis. For example, let's say we include each subject's individual exposure level as well as, for that subject, an average exposure level that applies to all members of a group. This will clarify the sources and magnitude of ecologic and cross level bias that might be present. And it allows us to separate biologic, contextual, and ecologic effects.

This is particularly useful in social epidemiology, infectious disease epidemiology, and in the evaluation of population level interventions.

## Effect estimation in ecologic studies

- In individual level studies, effects are usually estimated by comparing the rate or risk of disease for exposed and unexposed populations
- In ecologic studies, we cannot estimate effects directly because we do not know the joint distribution within groups
  - In the table below, we only know the total columns, not a, b, c, or d

	Disease	No Disease	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
Total	a+c	b+d	N

 Joint  
 Marginal distribution

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One solution to the problem of separating individual and contextual effects, that is, these kind of group level effects, is to incorporate both individual and ecologic measures in the same analysis. For example, let's say we include each subject's individual exposure level as well as, for that subject, an average exposure level that applies to all members of a group. This will clarify the sources and magnitude of ecologic and cross level bias that might be present. And it allows us to separate biologic, contextual, and ecologic effects.

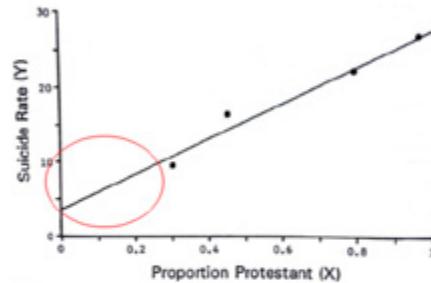
This is particularly useful in social epidemiology, infectious disease epidemiology, and in the evaluation of population level interventions. Let's talk a little bit about effect estimation in ecologic studies. Think first about individual level studies, the type we've studied so far in the course, where we measure individuals, we measure their exposure at the individual level and we measure their outcome at the individual level. In these types of studies, effects are usually estimated by comparing the rate or risk of disease for the unexposed and the exposed population separately and then comparing them.

For example, I have a group of smokers, that's one population, and a group of nonsmokers, that's another population. I compare the rates of cancer in the two groups, that's an individual level study comparing these two groups to each other but with individual level data. However, in ecologic studies, we can't estimate effects directly because we don't know the joint distribution within groups. And by joint distribution, I mean we don't know which exposed people have disease, which unexposed people have disease or don't have disease. All we know is that the population level, and in this table we've called it the marginal distribution here. We just know the total number of exposed and unexposed people and not which of those had disease or not disease.

Similarly, we know the total number of people with disease and without disease, but in those groupings we don't know who was exposed and who was unexposed.

## Effect estimation in ecologic studies

- A common approach is to regress the group-level disease rates on group-level exposure prevalence
- If the observed range of exposure prevalence or disease rates is narrow, we must be very careful about extrapolating beyond the range of the observed data since results may be highly dependent on the model chosen and its assumptions



Since there is no data on proportion Protestant  $< 0.3$ , any inferences about exposures at that level require extrapolation beyond the observed data.

How do we take these types of data and estimate effects in ecologic studies? One common approach is to regress the group level disease rates on the group level exposure or prevalence. For example, take a look at the figure you see here. This is plotting from work by Emile Durkheim, a sociologist. It's described in detail in your Rothman readings.

Look at the proportion of people who are Protestant in a population on the x-axis. That's going from zero to 100%. And you see the actual data points plotted as the dark dots there. On the y-axis, we're plotting the suicide rate in those different population. The four different dots are four different, actually, provinces in Bavaria. And we're looking at the specific suicide rate plotted against the proportion of the population that is Protestant. When you look at this graph and draw a regression line, you'd be tempted to conclude that as a place becomes more Protestant, there is more suicide, making you think that being Protestant is a risk factor for suicide.

However, the way this story really plays out is what was happening was in the areas that were more Protestant, it was actually Catholics who were committing suicide. As the area became more Protestant, it became more likely for Catholics living in the area with the higher proportion of Protestants to commit suicide because of group level effects that might have been discrimination or a feeling of isolation or many things like this that at the group level could be affecting individuals. But the conclusion that being Protestant was a risk factor was not correct. This ecologic regression, basically is giving us the opposite result what truly turned out to be the case.

## Confounders & effect modifiers in ecological analyses

- If group-level data on exposures and outcomes within levels of confounders / effect modifiers are available, two common approaches are used to adjust for confounding:
  - Include confounder/effect modifier in the statistical model
  - Standardize the disease rate for the confounder
- Requires marginal distribution within levels of confounder/effect modifier:

Confounder level Z=0

	Disease	No Disease	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
Total	a+c	b+d	N

Confounder level Z=1

	Disease	No Disease	Total
Exposed	a	b	a+b
Unexposed	c	d	c+d
Total	a+c	b+d	N

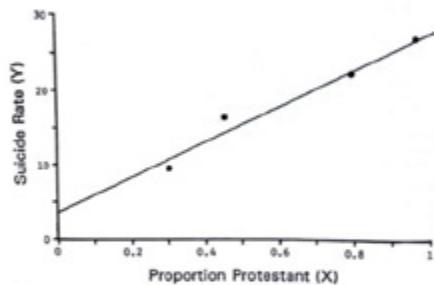
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Another issue is how to deal with confounders and effect modifiers in ecological analyzes. This is also complicated. So if we have group level data on exposures and outcomes within levels of confounders or effect modifiers, there are two common approaches used to adjust for confounding. We can include the confounder or effect modifier in this statistical model. Or we can standardize the disease rate for that confounder. But to do this, we have to have the marginal distribution within the levels of the confounder or effect modifier. You see here is an attempt to do this by stratifying some population into two strata, one stratum that doesn't have the confounder and one stratum that does. And then doing the estimation in each of the separate strata.

## Bias & confounding in ecologic studies

- **Ecologic bias:** failure of ecologic associations to reflect the biological effect at the individual level
- Heterogeneity of exposure level and covariate level within groups since the joint distribution is not available
- Example: ecological analysis estimated RR=7.6 for % Protestant and rate of suicide
  - None of the regions were 100% Protestant or non-Protestant
  - Without the joint distribution, we cannot know if suicides were among Protestants or non-Protestants



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Ecologic bias is a concept or a term used to refer to this phenomenon we saw earlier in the Durkheim graph where, at the population level, the association we thought we saw between being Protestant and suicide was not the actual biologic effect, in which there was actually more Catholics committing suicide. Heterogeneity of exposure level and covariate level within groups since the group distribution is not available is what causes this problem to occur. For example, here the ecological analysis estimated a relative risk of 7.6 for percentage Protestant and the rate of suicide. In other words, this regression concludes that Protestants are 7.6 times more likely to commit suicide than Catholics.

Note in this graph, none of the regions had fully 100% Protestant or non-Protestant populations. The conclusion about what's happening at the 100% or 0% level here has to be done from this regression line extending out to that level. Without the joint distribution of exposure and disease, we can't know whether the suicides were among Protestants or non-Protestants. But I've told you separately that it, in fact, it was the Catholics in the higher Protestant areas that were committing more suicide.

## Sources of ecologic bias

1. **Within-group bias:** bias results from bias within groups due to confounding, selection methods, or misclassification
  - Possible in any study
2. **Cross-level bias:**
  - **Confounding by group:** bias occurs if the background rate of disease in the unexposed population varies across groups
    - i. Unique to ecologic analysis
  - **Effect modification by group (on an additive scale):** bias results if the rate difference for the exposure effect at the individual level varies across groups
    - i. Unique to ecologic analysis

There are a couple different sources of ecological bias in ecological studies. Let's talk about within group bias and cross level bias. Within group bias arises due to confounding or selection methods or misclassification. This can occur in any type of study. And then cross level biases in the situation where we have confounding that occurs because of the groupings. Bias occurs if the background rate of disease in the unexposed population varies across groups.

This is a unique bias to ecologic studies. And also, there can be effect modification by the group on an additive scale. Bias here results if the rate difference or the exposure effect at the individual level varies across groups. And again, this is unique to ecological analysis.

## Example of when cross-level bias is present

Number of New Cases, Person-Years (P-Y) of Follow-up, and Disease Rate (Y, per 100,000y), by Group and Exposure Status (x) (top); Summary Parameters for Each Group (middle); and Results of Individual-Level and Ecologic Analyses (bottom): Hypothetical Example of Ecologic Bias due to Effect Modification by Group

Exposure Status (x)	Group 1			Group 2			Group 3		
	Cases	P-Y	Rate	Cases	P-Y	Rate	Cases	P-Y	Rate
Exposed (x = 1)	20	7,000	286	20	10,000	200	20	13,000	154
Unexposed (x = 0)	13	13,000	100	10	10,000	100	7	7,000	100
Total	33	20,000	165	30	20,000	150	27	20,000	135
Percentage of exposed (100X)		35			50				65
Rate difference (per 10 <sup>5</sup> y)		186			100				54
Rate ratio		2.9			2.0				1.5
Individual-level analysis				Ecologic analysis: linear model					
Crude rate ratio <sup>a</sup> = 2.0				$\hat{Y} = 200 - 100X (R^2 = 1)$					
Adjusted rate ratio (SMR) <sup>b</sup> = 2.0				Rate ratio = 0.50					

<sup>a</sup> Rate ratio for the total population, unadjusted for group.

<sup>b</sup> Rate ratio standardized for group, using the exposed population as the standard.

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Let's work through an example when cross level bias is present and not present to make the distinction here. This is a hypothetical example where we know everything about this population.

We have these three different groups that allow us to compare at the individual level what the risk of exposure is compared to non-exposure. If we don't adjust for the differences in groups, that is, we combine all group one, two, three together, if you do that, you'll come up with a crude rate ratio of 2.0. This would just come from collapsing group one, two, and three together, looking at the rates of disease in the exposed group and the rates and the unexposed group and you'd get a crude rate ratio of 2.0.

If you adjusted by standardizing for the three groups, and that's a technique we've worked with earlier in the course, you would also come up with a standardized mortality ratio of 2.0. However, when you do an ecologic analysis and you plot y versus x here where y is the rate of disease for the three groups and x is the proportion exposed on the x-axis, you'll find that the rate ratio now is only 0.50.

Clearly, the ecological analysis is very much in the wrong direction. It shows a lessening of risk whereas the individual level analysis and the crude analysis at the individual level suggests a doubling of risk. Clearly, the ecological analysis here is flawed.

## Example of when cross-level bias is absent

Number of New Cases, Person-Years (P-Y) of Follow-up, and Disease Rate (Y, per 100,000y), by Group and Exposure Status (x) (top); Summary Parameters for Each Group (middle); and Results of Individual-Level and Ecologic Analyses (bottom): Hypothetical Example of No Ecologic Bias

Exposure Status (x)	Group 1			Group 2			Group 3		
	Cases	P-Y	Rate	Cases	P-Y	Rate	Cases	P-Y	Rate
Exposed (x = 1)	16	8,000	200	30	10,000	300	24	12,000	200
Unexposed (x = 0)	12	12,000	100	20	10,000	200	8	8,000	100
Total	28	20,000	140	50	20,000	250	32	20,000	160
Percentage of exposed (100X)		40			50			60	
Rate difference (per $10^5$ y)		100			100			100	
Rate ratio		2.0			1.5			2.0	
Individual-level analysis				Ecologic analysis: linear model					
Crude rate ratio <sup>a</sup>				$\hat{Y} = 133 + 100X$ ( $R^2 = 0.029$ )					
Adjusted rate ratio (SMR) <sup>b</sup>				Rate ratio = 1.8					

<sup>a</sup> Rate ratio for the total population, unadjusted for group.

<sup>b</sup> Rate ratio standardized for group, using the exposed population as the standard.

Now let's move on to an example where there's no cross level bias. Here's another hypothetical example with three groups in which the crude rate ratio and the adjusted rate ratio are both 1.8 but the ecologic analysis also here turns out to give us a rate ratio of 1.8 as well.

So there's no ecologic bias here in this result. But the problem is, you can't know this ahead of time when you go out and you analyze the actual empiric data.

## Summary of key points

- Despite the drawbacks of ecologic studies, there are certain types of data and research topics for which they are advantageous.
- Ecological studies can compare rates between groups, between time periods, or both.
- Ecological analyses can adjust for confounders and effect modifiers.
- In all ecological studies, we must be careful to make appropriate inferences and minimize bias to the extent possible.

Let's summarize the key points about an ecological study. Despite the drawbacks of ecologic studies, there are certain types of data and research topics for which they're advantageous. They allow us to compare rates between groups, between time periods, or both. They can adjust for confounders in effect modifiers if we have them at the group level. And in all ecological studies, we have to be careful to make appropriate inferences and minimize bias to the extent possible.

## ORIGINAL ARTICLE

# Acute Changes in Community Violence and Increases in Hospital Visits and Deaths From Stress-responsive Diseases

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AQ1

**Background:** Community violence may affect a broad range of health outcomes through physiologic stress responses and changes in health behaviors among residents. However, existing research on the health impacts of community violence suffers from problems with bias.

**Methods:** We examined the relations of acute changes in community violence with hospital visits and deaths due to stress-responsive diseases (mental, respiratory, and cardiac conditions) in statewide data from California 2005–2013. The community violence exposure was measured as both binary spikes and continuous acute changes. We applied a combined fixed-effects and time-series design that separates the effects of violence from those of community- and individual-level confounders more effectively than past research. Temporal patterning was removed from community violence rates and disease rates in each place using a Kalman smoother, resulting in residual rates. We used linear regression with place fixed-effects to examine within-place associations of acute changes in community violence with residual rates of each outcome, controlling for local time-varying covariates.

**Results:** We found acute increases in hospital visits and deaths due to anxiety disorders (0.31 per 100,000; 95% confidence interval [CI] = 0.02, 0.59), substance use (0.47 per 100,000; 95% CI = 0.14, 0.80), asthma (0.56 per 100,000; 95% CI = 0.16, 0.95), and fatal acute myocardial infarction (0.09 per 100,000; 95% CI = 0.00, 0.18) co-occurring with violence spikes. The pattern of findings was similar for the exposure of continuous acute violence changes.

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The data are available from the State of California upon request for research purposes. We do not have the authority to share the data. Analysis code, in the program R, is provided in eAppendix 4 to facilitate replication or building upon our research.

The results reported herein correspond to the aims of grant DP2HD080350 to investigator J.A. from the National Institutes of Health. This work was also supported by pilot grant funds from the Robert Wood Johnson Health and Society Scholars Program and the University of California, Berkeley Committee on Research. Analyses, interpretations, and conclusions are those of the authors and not those of the California Department of Public Health or the National Institutes of Health.

**AQ2** The authors report no conflicts of interest.

**SDC** Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article ([www.epidem.com](http://www.epidem.com)).

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**Conclusions:** Although the associations were small, the identified increases in stress-responsive conditions suggest the possibility of health impacts of acute changes in community violence.

**Key Words:** anxiety disorders, asthma, California, hospital visit, myocardial infarction, residence characteristics, violence, vital statistics

(*Epidemiology* 2018;29: 00–00)

Community violence, which includes injuries due to assault and deaths due to homicide, is a major public health concern.<sup>1–3</sup> Research suggests that community violence may affect a broad range of health outcomes. Thus, the scope of public health concern around community violence may extend beyond injury.

Theory and research support an important role of the contextual environment in shaping the health of residents.<sup>4–7</sup> Community violence is recognized globally as an important aspect of the contextual environment.<sup>2</sup> Residents can experience community violence as direct injury, injury of friends or family, witnessing violence, hearing gunshots, and learning about violence through neighbors or media.<sup>8,9</sup> Research indicates that the rate of violence in a community strongly correlates with the frequency of experiences of direct injury and witnessing violence reported by residents.<sup>10,11</sup>

Furthermore, community violence can lead to stress for residents due to worry about harm to self, family, and friends; it can also lead to alterations in behavior that aim to keep the individual and family safe (e.g., staying inside, closer monitoring of youth, or avoiding parts of communities).<sup>12–14</sup> Community violence may affect residents' health through changes in behaviors such as physical inactivity, unhealthy diets, and substance use, in an effort to stay safe or cope with stress.<sup>15,16</sup> Physiologic aspects of the stress response, such as the activation and disruption of the hypothalamic–pituitary–adrenal axis and the alteration or increase in systemic inflammatory response, may also impact the health of residents.<sup>17–20</sup>

Based on established links between community violence and both physiological and behavioral stress responses, it is reasonable to consider the potential for health impacts of community violence on stress-responsive diseases. Indeed, a

variety of studies have found associations between community violence exposure and mental health.<sup>21–35</sup> There is also evidence that community violence may exacerbate asthma and increase the risk of heart conditions.<sup>36–45</sup> Across conditions, there are behavioral and biologic mechanisms through which exposure to community violence would increase both incidence of disease and acute exacerbations among those with existing disease.

There are major methodologic limitations in research to date on the health effects of community violence. Same-source bias occurs when self-report of both exposure and outcome leads to spurious association due to correlated measurement error in the report (e.g., due to optimistic or pessimistic outlook of the respondent). Same-source bias is a concern in studies that rely on self-report of community violence exposure and associate it with self-reported health outcomes.<sup>46</sup> In studies that limit same-source bias by using a separate data source for violence exposure, the strong correlation of community violence with other important determinants of health, such as economic, social, and physical features of communities, creates problems with structural confounding.<sup>47</sup> Structural confounding occurs when the correlation between the exposure and covariates is too strong to separate the effects. Thus, disentangling the effects of community violence from other determinants of health has posed a major challenge.

Violence varies substantially within communities over short time-frames. These acute changes in community violence offer an opportunity to overcome structural confounding challenges. A comparison of health outcomes at times with higher and lower levels of acute violence in the same geographic area allows each place to serve as its own control. This approach separates the effects of violence from other economic, social, and physical characteristics of places and individuals that remain constant within places over the study period.

In this study, we examined the associations of two forms of acute community violence, specifically binary spikes and continuous acute changes, with hospital visits and deaths due to stress-responsive diseases throughout California, using a combined fixed-effects and time-series design. The diseases included a range of mental, respiratory, and cardiovascular disorders that previous research suggests may be exacerbated by stress. We hypothesized that acute increases in community violence would increase these health outcomes.

## METHODS

### Data

To capture both fatal and nonfatal occurrences of community violence and of the outcome diseases of interest, we used two statewide data sources for California between 2005 and 2013. For fatal outcomes, we used all mortality records from the California Department of Public Health Office of Vital Statistics. For nonfatal outcomes, we used all emergency

department and inpatient hospitalization discharge records from California's Office of Statewide Health Planning and Development (OSHPD). Events that resulted in fatality in the OSHPD data were removed to avoid double counting. The research was reviewed and approved by the Committees for the Protection of Human Subjects at the University of California, Berkeley, and OSHPD. We used US Census Bureau population estimates as denominators and calculated monthly rates at the census-designated place level (hereafter "place"). Places are single, locally recognized, settled concentrations of residents that are named but do not have to be legally incorporated.<sup>48</sup> We selected places because, as the named cities and towns in which people reside, information about an unusually high level of violence in a month would be expected to be known within the area. These units are also large enough for stable estimation of monthly rates of community violence and the outcomes of interest. Consistent with other research, we examined places with at least 5,000 residents to ensure stable rates of both community violence and the outcomes of interest<sup>49</sup>; based on this restriction, 91% of California residents (~34 of ~37 million people) residing in 42% of places (631/1,516 places) were included.

### Acute Changes in Community Violence

Monthly rates of community violence were calculated as the rate of homicides and assaults, identified by ICD codes as detailed in Table 1. We applied a Kalman smoother to each place-level 108-month series, resulting in residual rates, which retain variability in community violence that was not predictable based on the temporal patterning of the time-series.<sup>50</sup> Temporal patterns removed include secular trends, cycles, and seasonality. Residuals from the Kalman smoother model fit constituted the exposure of continuous acute changes in community violence. Binary spikes in community violence were operationalized as place-months with residuals from the Kalman smoother that were greater than two standard deviations above the series. In a simulation study of time-series methods for spike identification, the Kalman smoother performed best in correctly identifying spikes while minimizing false positives (for example: 90.0% sensitivity and 99.4% specificity for spikes of 50% above the average rate; 84.6% sensitivity and 99.1% specificity for spikes of 40% above the average rate; Goin et al, Unpublished Data, 2017).<sup>50</sup>

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### Health Outcomes

Monthly rates of the health outcomes of anxiety disorders, episodic mood disorders, substance use, asthma, chronic obstructive pulmonary disease (COPD), acute myocardial infarction (MI), and heart failure were calculated based on International Classification of Diseases (ICD) codes as detailed in Table 1. For each outcome group, we examined all events (fatal and nonfatal combined) and fatal events alone when sufficient numbers of fatal outcomes occurred for model convergence. As with the community violence exposure, predictable temporal patterning was removed from disease rates

**F1** in each place with a Kalman smoother.<sup>50</sup> The Figure presents an example of substance use rates with the Kalman smoother fit and the residual rates after processing.

## Design

In a combined fixed-effects and time-series design,<sup>51,52</sup> within each place we compared (1) outcomes in months with a violence spike to the outcomes in months without a spike and (2) outcome changes associated with continuous acute violence changes across months. Comparing outcomes in the same geographic area allowed us to separate the effects of the acute violence from the effects of other economic, social, and physical characteristics of places and individuals that are constant over this time period within a place. However, shared

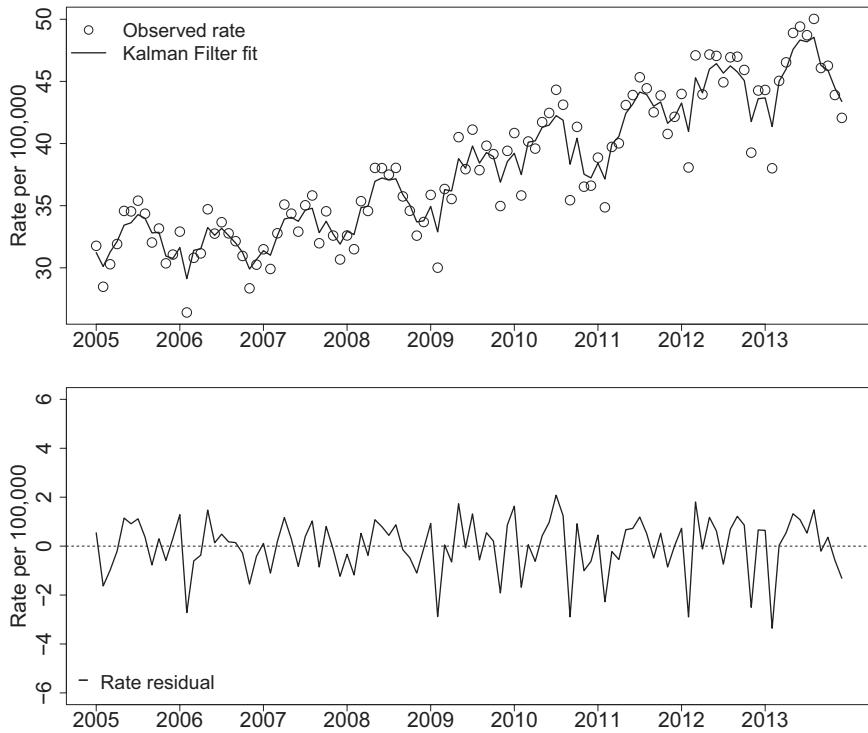
temporal patterning in the acute violence and outcomes remains a concern. Thus, for all analyses, dependent variables were Kalman smoother residuals of the outcome rates, so that we only examine variability in the outcomes that was not predictable based on the temporal patterning of the time-series.<sup>50</sup> This approach removes local temporal patterning specific to each place and, thus, provides control for confounding by local variables with predictable patterning.<sup>53</sup>

## Analysis

Analyses were conducted with linear regression models with fixed-effects on place and robust sandwich standard errors.<sup>54</sup> We adjusted for local monthly average precipitation, average temperature, unemployment, and civil unrest events

**TABLE 1.** ICD Codes Used to Classify Hospital Discharge and Mortality Records for Measures of Violence and Health Outcomes

Measure	ICD-9 (Hospital Discharge Records)	ICD-10 (Mortality Records)
Homicides and assaults	E960-E969, E970-E977	X85-X99, Y00-Y09, Y35, U01, U02, Y871
Anxiety disorders	300 and all 300 subtypes, 308-309 and all 308-309 subtypes	F40-F45 and all F40-F45 subtypes, F48 and all F48 subtypes, F93.0-F93.2
Episodic mood disorders	296 and all 296 subtypes	F30-F34 and all F30-F34 subtypes, F38-F39 and all F38-F39 subtypes
Substance use	291-292 and all 291-292 subtypes, 303-305 and all 303-305 subtypes	F10-F19 and all F10-F19 subtypes
Asthma	493 and all 493 subtypes	J45 and all J45 subtypes, J46
Chronic obstructive pulmonary disease	490-492 and all 490-492 subtypes, 494 and all 494 subtypes, 496	J40-J44 and all J40-J44 subtypes, J47 and all J47 subtypes
Acute myocardial infarction	410 and all 410 subtypes	I21-I22 and all I21-I22 subtypes
Heart failure	428 and all 428 subtypes	I50 and all I50 subtypes



**FIGURE.** Rates of hospital visits and deaths owing to substance use to illustrate Kalman smoother fit and residuals, Los Angeles 2005-2013.

to control for confounding by covariates with unpredictable temporal patterning that change over short time-frames and are determinants of both community violence and health outcomes.<sup>55,56</sup> Additionally, we controlled for local annual measures of poverty, unemployment, marital status, racial/ethnic composition, and educational attainment that are strongly predictive of violence (see eAppendix 1; <http://links.lww.com/EDE/B373> for covariate details). We also conducted a sensitivity analysis in which we identified and omitted places from the analysis for a given outcome if there was evidence of persistent autocorrelation in the time-series. (See eTable 2; <http://links.lww.com/EDE/B373> and eAppendix 2; <http://links.lww.com/EDE/B373> for sensitivity analysis results). All analyses were conducted in R version 3.2.1 (see eAppendix 4; <http://links.lww.com/EDE/B373> for code).

## RESULTS

Across the 631 places over 108 months (68,148 place-months of observation), there were 2,401 violence spikes, and all but six places experienced at least one spike. For the continuous violence measure and each outcome, the distribution of the total cases, average monthly rates and monthly rate residuals after Kalman smoother processing across the place-months of analysis can be found in Table 2.

In the main analysis models that examined binary violence spikes in relation to residual outcome rates, including fixed-effects on place and control for time-varying local covariates (Table 3), we found acute increases in deaths and hospital visits due to anxiety disorders (0.31 per 100,000 increase; 95% confidence interval [CI] = 0.02, 0.59), substance use (0.47 per 100,000 increase; 95% CI = 0.14, 0.80), asthma (0.56 per 100,000 increase; 95% CI = 0.16, 0.95), and

fatal acute MI (0.09 per 100,000 increase; 95% CI = 0.00, 0.18) co-occurring with violence spikes. In the models that examined continuous acute violence in relation to residual outcome rates (Table 3), there was a similar pattern of results with acute increases in deaths and hospital visits due to anxiety disorders (0.14 per 100,000 increase; 95% CI = 0.04, 0.24), substance use (0.35 per 100,000 increase; 95% CI = 0.24, 0.46), and asthma (0.16 per 100,000 increase; 95% CI = 0.03, 0.30) for a 10 per 100,000 difference in acute violence. Continuous acute violence was not associated with fatal acute MI. Overall, there were no indications of changes in deaths and hospital visits due to episodic mood disorders, COPD, or heart failure associated with acute community violence.

In the sensitivity analysis, we first examined residual autocorrelation by outcome and for the exposure of community violence (eAppendix 2; <http://links.lww.com/EDE/B373> and eTable 1; <http://links.lww.com/EDE/B373>). In general, the degree of residual autocorrelation was low; however, autocorrelation tended to persist in the fatal asthma (20.9% of places) and fatal substance use (9.2% of places) time-series. For all other outcomes and the community violence exposure autocorrelation was minimal, with a few places for some outcomes in which autocorrelation persisted (range from 0% to 1.3% of places). In models that omitted places from the analysis for a given outcome if there was evidence of persistent autocorrelation in the time-series, the results were unchanged (eAppendix 2; <http://links.lww.com/EDE/B373> and eTable 2; <http://links.lww.com/EDE/B373>).

## DISCUSSION

Overall, we found acute relations of community violence with anxiety disorders, substance use, asthma, and fatal

**TABLE 2.** Description of Health Outcomes Across All Place-Months of Analysis, California 2005–2013

Condition	Outcome	Total Cases	Rate <sup>a</sup>		Rate Residuals <sup>b</sup>
			Mean	IQR	
Community violence	Combined fatal and nonfatal	1,124,382	27.2	13.08, 37.08	-3.68, 3.00
Anxiety disorders <sup>c</sup>	Combined fatal and nonfatal	922,064	25.5	14.40, 33.38	-3.65, 3.02
Episodic mood disorders <sup>c</sup>	Combined fatal and nonfatal	973,049	23.85	12.93, 32.35	-3.64, 2.85
Substance use	Combined fatal and nonfatal	1,255,735	32.32	18.432, 42.114	-4.21, 3.49
	Fatal only	8,338	0.247	0, 0	-0.14, -0.03
Asthma	Combined fatal and nonfatal	1,494,217	38.06	18.73, 51.30	-5.06, 4.08
	Fatal only	3,409	0.09	0, 0	-0.06, 0.00
Chronic obstructive pulmonary disease	Combined fatal and nonfatal	1,299,122	38.08	18.38, 49.16	-4.99, 3.82
	Fatal only	99,232	3.23	0, 4.50	-1.30, 0.66
Acute myocardial infarction	Combined fatal and nonfatal	538,233	15.86	7.96, 20.80	-3.15, 2.35
	Fatal only	92,961	2.68	0, 3.79	-1.15, 0.53
Heart failure	Combined fatal and nonfatal	828,778	22.63	12.72, 29.84	-3.49, 2.85
	Fatal only	37,283	1.15	0, 0.98	-0.58, 0.00

<sup>a</sup>Rates are per 100,000 population.

<sup>b</sup>Rate residuals all have a mean of zero.

<sup>c</sup>There were too few cases of these fatal outcomes to examine them separately (fatal anxiety disorder cases: 46, fatal episodic mood disorder cases: 322).

IQR indicates interquartile range.

**TABLE 3.** Relationships of Acute Violence Changes With Health Outcomes, Estimated With Linear Regression Analysis of Monthly Residual Outcome Rates With Fixed-effects on Place, California 2005–2013

Condition	Outcome	Residual RDs Associated With Violence Spikes <sup>a</sup>		Residual RDs Associated With Acute Violence Increases <sup>a,b</sup>	
		RD <sup>c</sup>	95% CI	RD <sup>c</sup>	95% CI
Anxiety disorders <sup>d</sup>	Combined fatal and nonfatal	0.31	0.02, 0.59	0.14	0.04, 0.24
Episodic mood disorders <sup>d</sup>	Combined fatal and nonfatal	0.07	-0.2, 0.35	0.07	-0.02, 0.17
Substance use	Combined fatal and nonfatal	0.47	0.14, 0.80	0.35	0.24, 0.46
	Fatal only	0.00	-0.02, 0.03	0.00	-0.01, 0.01
Asthma	Combined fatal and nonfatal	0.56	0.16, 0.95	0.16	0.03, 0.30
	Fatal only	0.00	-0.02, 0.01	0.00	0.00, 0.01
Chronic obstructive pulmonary disease	Combined fatal and nonfatal	0.02	-0.35, 0.38	-0.10	-0.25, 0.04
	Fatal only	0.00	-0.10, 0.10	-0.02	-0.05, 0.02
Acute myocardial infarction	Combined fatal and nonfatal	0.08	-0.16, 0.31	0.03	-0.05, 0.11
	Fatal only	0.09	0.00, 0.18	0.01	-0.02, 0.04
Heart failure	Combined fatal and nonfatal	0.23	-0.04, 0.49	0.00	-0.10, 0.09
	Fatal only	-0.01	-0.07, 0.04	-0.01	-0.03, 0.01

<sup>a</sup>Residuals based on fitting a Kalman smoother to the outcome rates in each place to remove predictable temporal patterning.<sup>b</sup>RD corresponding to 10 per 100,000 increase in acute violence residual.<sup>c</sup>Controlled for local monthly average precipitation, average temperature, unemployment, and civil unrest events; controlled for local annual measures of poverty, unemployment, marital status, racial/ethnic composition, and educational attainment.<sup>d</sup>There were too few cases of these fatal outcomes to examine them separately (fatal anxiety disorder cases: 46, fatal episodic mood disorder cases: 322).

RD indicates rate difference.

acute MI. Although studies have documented correlations of community violence with mental health and substance use outcomes,<sup>21–35</sup> our design provides stronger evidence by avoiding same-source bias and minimizing structural confounding. The findings are also consistent with the small set of studies that has examined the relations of community violence with asthma and cardiac events.<sup>36–45</sup>

Our exposures were acute changes in community violence and, thus, do not capture any effects of chronic exposure to community violence on the outcomes. The combined time-series and fixed-effects approach removes any effect of the average rate of violence and isolates the effect of acute violence changes. Chronic exposure to violence is also a stressor and expected to have important impacts on health, but these effects are more challenging to separate analytically from other community characteristics.<sup>57</sup> Thus, differences between our results and studies of violence rates may be attributable to our examination of only acute forms of violence.

There are several considerations for interpretation of the results with respect to the outcomes. Increases in cause-specific hospital visits and deaths may be composed more of exacerbations in underlying conditions than of incident outcomes. Furthermore, the outcomes include only events that are sufficiently serious to result in an emergency department visit, hospitalization, or death. Thus, we do not have data on less severe events or exacerbations of symptoms that influence health and well-being but do not necessitate a visit to the hospital or result in a death and may underestimate the overall burden associated with acute violence. However, we have captured the most

severe and costly events—a subgroup of interest and concern. Although health care coverage varies and may affect use of the hospital system,<sup>58</sup> this would only affect our results if temporal, within-place changes in health care coverage coincide with the acute violence changes during the study period.

We examined cities and towns as the geographical units of interest in this study. Although we expect that residents would be aware of violent events within this geography, it is possible that smaller areas would better capture the geographical scope in which violent events would generate concern or impact residents, particularly in larger cities. In general, results of geographic analyses may be sensitive to the choice of geographic unit, a problem that has been discussed as the modifiable areal unit problem.<sup>59</sup>

Among the substance use and mental disorders, acute violence was related to increases in deaths and hospital visits due to anxiety disorders and substance use, but not mood disorders. One explanation may be that exposure to traumas is more important for anxiety disorders, such as post-traumatic stress disorder, whereas determinants of mood disorders such as depression relate more to personal loss and supports available in the aftermath of the loss.<sup>60,61</sup> It is conceivable that an acute increase in violence could cause traumatic exposure for a broader population within a city or town, manifesting in increased hospital visits for anxiety and substance use. In contrast, acute violence would lead to personal loss for a much smaller subset of the population, and thus, increase in mood disorder-related hospital visits would be expected to be smaller and more challenging to detect at the population level.

The relationship of acute violence with cardiopulmonary outcomes was consistent for asthma but varied by form of acute violence for fatal MI. Research supports a clear role for chronic stress in the development and progression of cardiovascular diseases.<sup>42</sup> Acute stressors may induce acute cardiac events in those already physiologically vulnerable.<sup>42,43</sup> Although any explanation of inconsistency in findings is post hoc, it is worth noting that in research on population stressors that has found increases in acute cardiac events, the stressors have generally been of larger magnitude and/or of broader impact, specifically earthquakes, wars, and terrorist attacks.<sup>43</sup> Thus, it is plausible that acute changes in community violence had insufficient breadth, duration, and/or strength of impact to generate large enough effects on acute cardiac events for consistent detection in our analyses. Exacerbations of asthma, in contrast, are more frequent, and occurrence has been related to far less extreme acute stressors, such as exams.<sup>20</sup>

The magnitudes of association for the relations of violence spikes with the outcomes were small. With respect to the variability in the outcome residuals, the associations corresponded to between 2% and 6% of a standard deviation. As an example, statewide, the associations corresponded to an additional 120 anxiety, 183 substance use, and 218 asthma hospital visits and deaths and 35 fatal MIs in a month with a violence spike. However, a few considerations provide context for these magnitudes. These associations only capture acute increases in the most severe health events and thus may underestimate the overall burden associated with violence spikes. Furthermore, the associations only capture the changes in health outcomes associated with acute violence, not with the overall exposure to community violence. We would anticipate that the health outcome changes associated with the overall exposure to community violence to be much greater than those associated with acute spikes. However, as discussed above, we have approached this analysis with the aim of minimizing the types of confounding that plague past work on community violence and health. Thus, we viewed this as a test of whether, despite these strong control measures, a signal of a relation between acute violence and these health outcomes could be detected. Although a worthwhile endeavor to undertake in future work, capturing the true magnitude of the relation of community violence with health would require leveraging the full range of variability in violence, yet also controlling for strong structural confounders.

We examined outcomes in the same month as the violence spike because we hypothesized acute effects, but this raises a potential concern about the directionality of the associations. It is unlikely that increases in asthma or cardiac events would cause a violence spike. It is possible that increases in mental disorder or substance use could increase violence, since individuals who have a certain mental disorders or are using substances have increased risk of violent behavior.<sup>62</sup> However, at the population level, mental disorder is a very minor contributor to interpersonal violence (population

attributable risk percent [PAR%] estimate of 4%), and the anxiety and episodic mood-disorder outcomes examined here do not include personality disorders, which are most strongly associated with perpetration of violence.<sup>63</sup> Substance use is a more sizable contributor to perpetration of interpersonal violence at the population level than mental disorder (PAR% estimates range from 20% to 25%),<sup>63</sup> and, thus, the relation documented may represent effects of violence on substance use and effects of substance use on violence.

The largest threat to this analysis would be a cause of both acute violence changes and the health outcomes that varies unpredictably over short time spans within place and has not been controlled. However, we have identified and controlled for numerous common causes of acute changes in violence, and the health outcomes that may not follow predictable patterns. In particular, we controlled time-varying socio-economic, weather, civil unrest, and demographic variables at the local level. Nonetheless, residual confounding is always a concern in observational studies, particularly when associations are small.

Our approach assumes that past acute violence only affects future health outcomes within a place through more proximal acute violence and that past health outcomes within a place do not affect future acute violence changes.<sup>64</sup> In considering the first part of this assumption, although the underlying health conditions likely developed over a long period and may have been affected by prior acute violence, we are examining only acute changes in manifestations of these health conditions that are far less likely to be affected by prior acute violence. We evaluated the second part of this assumption by examining the relations of the health outcomes with subsequent acute violence changes within a place, and we found largely null associations (see eAppendix 3; <http://links.lww.com/EDE/B373>). This suggests that reliance on this assumption is reasonable in our study.

## CONCLUSIONS

Overall, our findings suggest that violence may affect health in the community more broadly, although magnitudes of associations were small. By examining acute changes in violence, using a design that controls for time-invariant confounders and incorporates careful control of predictable temporal patterning and observed factors that vary within place over time in ways that may not be predictable, we have strengthened the evidence for these potential health impacts.

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## Acute Changes in community violence and increases in hospital visits and deaths from stress-responsive diseases – Part 1

**MICHELLE RUIZ**

Hello welcome again to Epidemiology Case Studies Podcast. In this fourth episode you will hear Dr. Jade Benjamin-Chung interview Dr. Jen Ahern about an ecological study she conducted that explored whether community violence in California increased the risk of hospitalization.

**JADE BENJAMIN-CHUNG:** Hi, everyone. Today I'm going to be interviewing Professor Jennifer Ahern about a recent study she published, called Acute Changes in Community Violence and Increases in Hospital Visits and Deaths from Stress-Responsive Diseases. So thank you for being here.

**JENNIFER** You're welcome. I'm excited to be here.

**AHERN:**

**JADE BENJAMIN-CHUNG:** And I'm hoping we can begin by having you share how you became interested in this particular research question.

**JENNIFER** Sure. Well, I have sort of a longstanding interest in the effects of features of communities and

**AHERN:** how they affect health. And in the last, I don't know, 5 or 10 years, I started noticing in the context of the literature that community violence was one aspect of communities that had sort of been ignored in this.

And when you do a general survey in a community and you ask people, "what are the biggest issues for you?", violence is usually up in the top. Top 1, 2, 3 things. Often the top thing. Yet the world of thinking about community effects on health sort of hadn't addressed that. It's been thought of as a law enforcement issue or not a health issue.

And so some of our work in my group has been trying to apply rigorous designs to bring better evidence to the question of whether, in fact, community violence is a determinant of health in communities, and particularly health disparities in communities. And so that sort of-- this work falls within that area.

**JADE BENJAMIN-CHUNG:** And when you say community violence, what kinds of types of violence are you focusing on in this work?

**JENNIFER** So we have primarily been focusing on just sort of the out in the community, people are shot,

**AHERN:** someone's harmed in another way due to an assault. And obviously, that's not good for someone who's hurt directly, but there are lots of ways in which those sorts of high rates of those sorts of events in communities can affect the health of people who weren't actually directly harmed. And so that's sort of the mechanism through which we imagined this could be impacting health more broadly.

**JADE BENAMIN-CHUNG:** Can you talk a bit about what the sort of theory of causation is, from community violence leading to the health outcomes you chose to focus on in this research?

**JENNIFER AHERN:** Mhm. So there really are two categories of mechanism. One is around behavioral changes, and the other mechanism is around the stress-- physiologic stress response. And so we know that when stressful things occur there's a physiologic reaction, and that can have consequences for all kinds of diseases. And so that's sort of the one pathway.

So it's sort of over and over again you're having these events occur in the community. Sirens blaring. Worrying about who's in your family and where they are right now and all of that. This can cause a lot of stress for people.

And on the other side, there's a lot-- and there's a lot of biologically-based research documenting that those things occur in stressful situations. Then on the other side, we know that people make a lot of changes to how they behave if they live in a violent community. So for example, they will restrict where they move, maybe at all, during the day, and they will keep their kids indoors. They will avoid certain parts of the community completely on occasion.

And so if you just think about, you know, as an example, you might come home from work, and if you live in a community where you're not concerned about violence, it might be getting dark but you might think, oh, I can squeeze in a little jog or whatever. Whereas if you're in a community where violence is high, if it's starting to get dark, there's probably no way you're going to go out at that point. You're not going to take that risk on. So those are some examples of the kinds of things.

**JADE BENAMIN-CHUNG:** The paper title says it's focused on acute changes, and it also talks about the difference between acute and chronic stressors and sources of violence. So how did you decide to focus on the acute ones in this study?

**JENNIFER AHERN:** So we've done work on both. And as part of the bigger picture of the work, we wanted to parse out relationships that you can see from chronic violence and how that's related to health from those that you can see from acute, partly because that just hadn't been done really, and it's often somewhat conflated actually in the existing literature. So we wanted to be really clear about when we're looking at each form and how those are really distinct. And so this was just the part that was looking at the acute.

The designs we can use with looking at acute forms, I think, have some strengths.<sup>79</sup> And so

that's another reason that we're kind of separating them out, because it's a bit harder to look at chronic. And I wouldn't say it's easier to look at acute, but you get some design strengths if you focus on acute.

**JADE BENJAMIN-CHUNG:** That's a perfect transition to talking about the study design. So this article talks about a ecologic design, but it's actually quite a sophisticated ecologic design. Students often learn about ecologic designs as sort of the most risky in terms of worrying about validity.

**JENNIFER** That's right.

**AHERN:**

**JADE BENJAMIN-CHUNG:** So I'd love to hear about your choice of that design, and also, as an epidemiologist, how you think about ecologic designs for the kinds of research that you do.

**JENNIFER** OK, great. So I think the ecological design is sort of this like under-appreciated design that has

**AHERN:** strengths in particular types of situations. I think this paper is an example of a design where it has strengths. Often, when people say ecologic study, if you say that to a room of students, they like-- you say, what's the problem? And all the hands shoot up and they say, ecologic fallacy. And then you say, well, what do you mean by that? And they often can't articulate it.

They know there's something bad about ecological studies, but it's sort of become conflated, right? If it's this design, you have this fallacy and you should just not use it, or you should interpret with extreme caution.

But there's a really nice paper. I think it's Greenland. I don't have the reference in my head, but a Greenland paper from late '90s that really parses out, OK, ecologic design. What are the threats and what are the issues? And so when we say ecological fallacy, we usually mean-- what we should mean is that you infer an individual association from a group level association. To conflate those two would be the fallacy.

But in fact, sometimes our questions are interested in the effect of a group thing on an individual outcome. And there it isn't-- you're not in the same fallacy category. And what you're then worried about is whether you can adjust for confounding by composition of the population. And so in a study like the one we've done, the issue is, do we have to worry about the fact that over time the composition of this community might be changing?

And so we've overcome that challenge in a few ways here. One, we're making comparisons only within one community, and we're comparing times, I guess I should say, within each

community among a whole set of communities. And so that means in a given community, over the course of the year, sometimes violence spikes high, sometimes violence is not spiking high. And so we're really able to compare, often, adjacent times, where it's literally just a month of time has passed and one time happened to be a time of high violence and the other did not.

And so the extent to which you have to worry about, oh, is the age or race or gender distribution of this population changing dramatically over the frame? Well, if you're comparing adjacent months, suddenly you think, oh, well that's not such a threat in this design.

And the other big challenge in general with community comparisons is that when you compare across communities-- for example, a community that happens to be high violence a lot of the time and one that happens to be low violence-- there's so many things that are different between those communities, and it's very hard to adjust for it statistically without extrapolating. And so being able to instead of cross community compare, where we worry about all those what we think of as structural confounding problems-- where you just can't really pull apart all these different determinants of health-- by focusing within a community, again, if you're talking about adjacent months in the same community, you're not as worried about all these other determinants of health that are going to be so different between community, because within that community, over a short time frame, they're probably reasonably constant.

**JADE BENJAMIN-CHUNG:** So the main threat to validity in this design, then, is variables that would change very quickly--

**JENNIFER** Exactly.

**AHERN:**

**JADE BENJAMIN-CHUNG:** --over time within one community.

**JENNIFER** That's exactly right. And so we tried to brainstorm about what those things were that we

**AHERN:** should be worried about. So here an example would be something like the economy that does vary on a reasonably short time frame, and we could imagine that affecting violence and potentially affecting some of these health outcomes. And so those are the types of things. We also controlled acute weather changes, things like that.

**JADE BENJAMIN-CHUNG:** So weather is strongly associated with violence?

**JENNIFER** It is strongly associated with violence. There's sort of the obvious when it's raining<sup>81</sup>, people

**AHERN:** aren't out and about.

**JADE BENJAMIN-CHUNG:** Less happens.

**JENNIFER** Yeah. There's just less activity outdoors in terms of thinking about community violence. But

**AHERN:** we've also shown, in other work, sort of surprisingly persistent associations of just the ambient temperature with violence, which I guess sort of makes sense. As you get uncomfortably warm, your tolerance for all kinds of things probably goes down.

**JADE BENJAMIN-CHUNG:** So it's not only an ecologic design, but you also use the phrase "fixed effects" and "time series" to describe the design. Are those terms commonly used in epidemiology? I think I've heard them in the economics literature a little bit more.

**JENNIFER** That's right. Yeah. I mean, I think there's been a lot of sort of method sharing or method

**AHERN:** stealing, you could say, across disciplines over the last several years that I think is pretty productive for the most part. And so fixed effects approach is just the way in which we're able to limit ourselves to within community comparisons. We sort of condition on each community and estimate within each community by using a fixed effect.

And time series similarly comes a bit more out of the economics. Some other disciplines use it as well.

**JADE BENJAMIN-CHUNG:** Tell me about the data sources. Presumably, because you're using an ecologic study, you have population level data. But where did you get this information from, and how did you assemble all of it?

**JENNIFER** OK. This was part of a project that involved compiling a health database for the state of

**AHERN:** California. And one of the first steps was just figuring out what we could actually compile and what it would then be useful for doing. And what we've got in the database are all of the deaths in the state, all of the hospital system visits-- so that includes inpatient and emergency department visits to the hospital. And then, it was not part of this study, but we have all of the births in the state, as well as some files that are linked across births and hospital system. For example, the mother's hospitalization, as well as the birth record of the child who was born when she comes to deliver.

**JADE BENJAMIN-CHUNG:** That sounds like a large undertaking.

**JADE BENJAMIN-CHUNG:** And presumably you'll be using that not just for this analysis but for many.

**JENNIFER AHERN:** Yes. So it's sort of like data infrastructure that we're hoping can be leveraged to look at the health impacts of policies in programs in the state. In addition to trying to understand how violence affects health, the second piece of the project was looking at how programs and policies that relate to criminal justice and violence are impacting health in the state.

**JADE BENJAMIN-CHUNG:** How did you choose the particular outcomes that you focused on in this study?

**JENNIFER AHERN:** So we went through a very long process of trying to review a lot of literature on what was stress responsive, because we really wanted to not include conditions where there wasn't a plausible mechanism. And so we really went-- it's using hospital system data, so we're using ICD codes, which say, like, what did the person come in for? And we had a very long and somewhat tedious process of putting all the ICD codes up and talking about, where is there literature supporting each of these? And should this particular subtype be in versus out?

So we went through a lot of that before we actually went and looked to see what was going on. But it is interesting, because one of the things that came out in reviewing the literature is that there was a big category of things where there probably is some plausibility but we didn't feel like the literature was strong enough. So we didn't want to put it in, but we had hoped to follow this up with more of an exploratory study that did something more data adaptive, to be rigorous about looking for other outcomes where there wasn't literature. But we haven't gotten there yet. I don't know if we'll end up doing it or not.

**JADE BENJAMIN-CHUNG:** And it sounds like quite a few people were involved in this. How many people, and were they all epidemiologists, or did you have anyone from a different field?

**JENNIFER AHERN:** So pretty much the whole team were students and staff in the epidemiology division in the School of Public Health here at Berkeley, at least at the time. Some of them are now on to other things. But I will say that a lot of what we did was informed by work I've done collaboratively with people like Ray Catalano in the past, who's an economist, as well as with Will Dowd, who's an economist. So there's a lot of conversations and ideas that came out of other disciplines, even though the people directly involved were all in epidemiology.

**PRESENTER:** Great. Well, thanks for telling me about the study design. We're going to come back. And in the next interview, we'll talk about threats to validity and what the study found.