Kuwait Longitudinal Heath Study

Environment and Health in Kuwait

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Chronology of Harvard Involvement

- **1991**
  - Harvard researchers on ground measuring environmental impacts of oil fires
  - Organized international conference on health effects of oil fires and environmental contamination

- **2002**
  - Harvard selected by Public Authority for Assessment of Compensation to assess public health impacts of Iraq’s 1990 invasion, occupation, and assault on Kuwait environment and health care system

- **2003**
  - Initiated epidemiologic study of long term effects of the war, the Public Health Survey
Invasion and Occupation

- **2 August 1990** - Invasion
  - Normal vacation period
- **17 January 1991** – Air war
- **10 February 1991** – First Oil Fire
- **23 February 1991** – Ground War
- **26 February 1991** – Liberation
  - 7 month occupation
- **6 November 1991** – Last Oil Fires Extinguished

Unique Characteristics

- Complete registry of Kuwaitis from birth to death.
  - Records were carried safely out of the country
- Invasion during the traditional summer holidays
  - Substantial fraction of Kuwait population out of country
    - Fraction of the population directly exposed to the invasion and occupation
    - Complementary fraction outside of the country did not directly experience the invasion and occupation.
- Stipend to Kuwaitis who remained in country during invasion and occupation
  - Indicator of exposure to invasion and occupation.
- After liberation, Kuwaitis encouraged to return
  - Destroyed infrastructure restored
  - Health care and social support systems restored
  - Care and counseling provided
Kuwaiti National Population

576,861 Kuwaiti Nationals
- 16 Feb 1991
- Public Authority for Civil Information Records

Very Young Population
- 47% ≤ 10 Years
- 75% ≤ 25 Years

Many outside of Kuwait during Occupation
- 37% received Stipend for being in Kuwait
- ~ 50% in Kuwait when fires began
- ~ 95% in Kuwait when fires ended

Population Mortality
- Public Authority for Civil Information (PACI)
  - Database of all Kuwaiti nationals alive on the date of liberation (26 February 1991).
- Matched to Ministry of Finance records of those who had received stipend.
  - In-county - those who received stipend for remaining in Kuwait during the entire invasion and occupation.
  - Out-of-country - those who did not request or receive stipend
- Matched by Civil Identification Number to PACI records of date of death (1991 to 2003).
  - No cause of death
Kuwait Nationals Population

<table>
<thead>
<tr>
<th></th>
<th>In country</th>
<th>Out of country</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>212,565</td>
<td>364,296</td>
</tr>
<tr>
<td>Person-years</td>
<td>2,527,231</td>
<td>4,363,499</td>
</tr>
<tr>
<td>Deaths</td>
<td>10,283</td>
<td>12,357</td>
</tr>
<tr>
<td>% deaths population</td>
<td>4.8%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Deaths/1000 person-years</td>
<td>4.07</td>
<td>2.83</td>
</tr>
</tbody>
</table>

- Cox PH regression controlled for age, sex, and age*sex interactions
  - HR 1.17 (95% CI 1.14, 1.20) p<0.0001

Public Health Survey I

- Living Kuwaiti nationals 50 to 69 years on date of invasion.
- Random sample stratified by gender, age, and in-country and out-of-country.
- Contacted by phone and asked to participate.
  - Written informed consent
- Face-to-face interviews at home between 3 December 2003 and 29 January 2005.
  - Next of kin for deceased or those unable to answer
- Questionnaire
  - residence during the invasion and occupation,
  - experiences during the occupation,
  - medical conditions and health care utilization before and after the occupation,
  - date of death for deceased subjects.
Public Health Survey

- Exposures during invasion and occupation
  - Self-reports of location
    - In or Out of Kuwait
    - Estimation of exposure to oil fire pollution
  - Self-reports of exposure to violence (as in previous studies)
    - Violence to self
    - Witnessed violence on family or others
    - In hiding (fear)

Public Health Survey

- Health events before and after invasion and occupation
  - Mortality
    - Date but not cause
  - Self-reports of physician diagnosed disease
    - Date of diagnosis
  - Self-reports of symptoms
  - Self-reports of hospitalizations
    - Dates and diagnoses
Public Health Survey

- Individual predictors of disease
  - Age and Gender
  - Self-reports of socioeconomic status
  - History of smoking
  - History of chronic diseases
  - Obesity indicators
    - Current Body Mass Index
    - Body type currently and prior to invasion
  - Diet and exercise

Survival of PHS Participants

*Adjusted for sex, age, smoking, education, income, and chronic illness*

HR 1.28 (95%CI 1.13, 1.44) p<0.0001
Hazard Ratio for Cause Specific Death:
Ever In vs Always Out of Kuwait During Invasion and Occupation

<table>
<thead>
<tr>
<th>ICD9</th>
<th># Deaths</th>
<th>HR</th>
<th>(95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Deaths</td>
<td>1573</td>
<td>1.28</td>
<td>(1.13,1.45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unknown</td>
<td>344</td>
<td>0.97</td>
<td>(0.76,1.24)</td>
<td>0.79</td>
</tr>
<tr>
<td>Circulatory</td>
<td>390-459</td>
<td>686</td>
<td>1.39 (1.15,1.69)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>140-239</td>
<td>183</td>
<td>1.41 (0.97,2.04)</td>
<td>0.071</td>
</tr>
<tr>
<td>Endocrine</td>
<td>240-279</td>
<td>95</td>
<td>1.31 (0.80,2.14)</td>
<td>0.29</td>
</tr>
<tr>
<td>Respiratory</td>
<td>460-519</td>
<td>67</td>
<td>1.91 (0.94,3.88)</td>
<td>0.076</td>
</tr>
</tbody>
</table>

Estimates of PM$_{2.5}$ Exposure

- CalPUFF Model to Estimate Exposure of Kuwaiti Nationals
  - Computed Plume Rise From Thermodynamics of Oil Fires
  - Used Improved Meteorological Data and Finer Grid Spacing
  - Accounted for Coastal Effects and Considered Plume Enhancement
- Values Vary Across Country and By Day
- Typical Values ~ 40-50 μg/m$^3$ (in populated areas)
- High Days 600 - 800 μg/m$^3$ (in populated areas)
- Estimated 0.1% increase in deaths from oil fires (p=0.46)
Public Health Survey Results

- Effect of self-reported exposure to violence
  - Attacked or Witnessed Attack (1468 subjects, 30%)
    - Personally arrested or attacked (6%)
    - Witnessed violence to family member (24%)
  - In Kuwait/Hiding (2164 subjects, 44%)
    - In hiding for 3 or more days (6%)
    - In Kuwait but no specific exposure to violence (39%)
  - Out of Kuwait (1254 subjects, 26%)
    - Out of Kuwait entire time (26%)

PHS-I PARTICIPANTS REPORTING WITNESSING SPECIFIC WAR-RELATED EVENTS

[Bar chart showing the percentage of participants reporting various war-related events by gender.]
Survival of PHS participants in Kuwait by reported exposure to violence

Adjusted for gender, age, smoking, income, and education

Coronary Heart Disease in PHS participants by reported exposure to violence

Adjusted for gender, age, smoking, income, and education
Chronic Obstructive Pulmonary Disease or Asthma in PHS participants by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>COPD or Asthma</th>
<th>P=0.01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out of Kuwait</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>In Kuwait or Hiding</td>
<td>1.0</td>
<td>P=0.54</td>
</tr>
<tr>
<td>Attacked or Witnessed Violence</td>
<td>1.6</td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education

Colitis in PHS participants by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>Colitis</th>
<th>P=0.06</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out of Kuwait</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>In Kuwait or Hiding</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Attacked or Witnessed Violence</td>
<td>1.6</td>
<td>P=0.01</td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education
Any Cancer in PHS participants by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>Out of Kuwait</th>
<th>In Kuwait or Hiding</th>
<th>Attacked or Witnessed Violence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>0.6</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>P = 0.76</td>
<td>P = 0.33</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education

Post Traumatic Stress Disorder in PHS participants by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>Out of Kuwait</th>
<th>In Kuwait or Hiding</th>
<th>Attacked or Witnessed Violence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>0.6</td>
<td>1.2</td>
<td>1.8</td>
</tr>
<tr>
<td>P = 0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education
Role of Trauma and Stress:
Heart Attacks and PTSD – PHS Phase I

- Incidence of heart attacks greater among those who experienced symptoms of PTSD.

- PTSD defined by presence of symptoms in at least two of four groups:
  - Troubled by unwanted memories or vivid dreams
  - Avoid things which remind you of the past
  - Feel emotionally numb
  - Irritable or “on edge”

Survival of PHS participants in Kuwait during invasion and occupation by reported exposure to violence

- Decreased Survival

Adjusted for gender, age, smoking, income, and education
Coronary Heart Disease in PHS participants in Kuwait during invasion and occupation by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>In Kuwait</th>
<th>In Hiding</th>
<th>Witnessed Violence</th>
<th>Attacked or Arrested</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>2.0</td>
<td>1.0</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>P-value</td>
<td>0.18</td>
<td>0.14</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education

Chronic Obstructive Pulmonary Disease in PHS participants in Kuwait during invasion and occupation by reported exposure to violence

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>In Kuwait</th>
<th>In Hiding</th>
<th>Witnessed Violence</th>
<th>Attacked or Arrested</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>P-value</td>
<td>0.72</td>
<td>0.008</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for gender, age, smoking, income, and education
Public Health Study- II
Phase II – Children and Their Parents

Select families with 2 children meeting age criteria

Recruit Mother And Father

Total sample 1800 Families 7200 Individuals

年龄入侵时

Father N=1800
Mother N=1800
Child N=1200
Child N=1200
Child N=1200

年龄
0-3 yrs
4-7 yrs
8-11 yrs

PHS II Questionnaires

- Individual Characteristics
  - Age, sex
  - Height and weight
  - Smoking
  - Diet and exercise
- Medical history
- Date of death
  - (Deceased only)
- Location
  - During invasion, occupation and oil fires
- Social/Psychological
  - Current functioning
  - Depression and anxiety Checklist
  - Gulf War Syndrome
  - Social network and support
  - Coping strategies
- Traumatic events
  - Before and After occupation
  - During occupation
- 64% Participation

RAC-GWVI Meeting Minutes
June 29-30, 2009
Page 43 of 248
PHS Biologic Markers

- **Anthropometry**
  - Height, Weight, and Blood pressure

- **Clinical Measures** (fingerstick, 89% participation)
  - Immediate reading
    - Total cholesterol, HDL, LDL, triglycerides
    - Blood glucose (random)
  - HgbA1C (**blood sugar control**)
  - C-reactive protein (**systemic inflammation**)

- **Future genetic testing**
  - Blood drops stored on treated filter paper

- **Hair sample** (**60% of possible**)
  - Environmental metals (**mercury**)

- **Salivary cortisol** (**Children** only, **37% participation**)
  - Measure of stress response

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Public Health Survey

**PHS I**

- **Men**
  - 63-82 yrs
  - N=2631

- **Women**
  - 63-82 yrs
  - N=2397

- **Generation I**
  - N=5028

**PHS II**

- **Father**
  - 50-78 yrs
  - N=1531

- **Mother**
  - 50-78 yrs
  - N=2286

- **Generation II**
  - N=3817

- **Child**
  - 16-19 yrs
  - N=1278

  - 20-23 yrs
  - N=1343

  - 24-27 yrs
  - N=1322

- **Generation III**
  - N=3943
Mean BMI vs Mean Age by Generation
PHS I and II

% Type II Diabetes vs Mean Age by Generation
PHS I and II
Cardiovascular Disease

Diagnosed Psychiatric Disorders
### Gulf War Syndrome Questions

#### Questions About Your Health

Please indicate below if you have had a persistent problem with each of the following symptoms over the past six months. If you have had the problem, please rate it as mild, moderate, or severe and indicate if it first became a problem before you deployed to the Gulf, or during or after your deployment.

<table>
<thead>
<tr>
<th>Over the past six months, have you had a persistent problem with .... ?</th>
<th>IF YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Mark NO or YES for each)</td>
<td>How would you rate this problem? When did you first have this problem? Before Gulf Deployment During or After Gulf Deployment</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Feeling unwell after physical exercise or exertion</td>
<td></td>
</tr>
<tr>
<td>Problems getting to sleep or staying asleep</td>
<td></td>
</tr>
<tr>
<td>Not feeling rested after you sleep</td>
<td></td>
</tr>
<tr>
<td>Pain in your joints</td>
<td></td>
</tr>
<tr>
<td>Stiffness in your joints</td>
<td></td>
</tr>
<tr>
<td>Pain in your muscles</td>
<td></td>
</tr>
<tr>
<td>Body pain, where you hurt all over</td>
<td></td>
</tr>
</tbody>
</table>

### Gulf War Syndrome Questions

الجزء II: ظاهرة حرب الخليج

هذه قائمة من الأعراض التي يمكن أن تكون أحيانًا جزءًا من ظاهرة "وشك في". إذا كنت تعتقد أن هذه الظاهرة حدثت لك في المدة التي تتبعها لفترة وكنت تعتقد أن هذا هو الأولى مرة قبل الهجوم العراقي على الكويت في 2 أغسطس 1990، أو بعد هذا التاريخ.

<p>| عبر السنة الأشهر الماضية، هل كان لديك مشكلة دائمة مع .........؟ |
|---------------------------------------------------------------|-------------------------|
| كيف تقيم هذه المشكلة؟ (ضع تعليمة عند لا أو تعليمة وحدة)      | نعم لا                     |
| هذا الشكل المحدد في عربي بمهما كان تدريجياً أو التدريجية |                         |
| متوسطة ومنخفضة                                             |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |
| عالية ومنخفضة                                               |                         |</p>
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Severity</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td></td>
<td>21%</td>
<td>8%</td>
</tr>
<tr>
<td>Unwell after exercise</td>
<td></td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Sleep Problems</td>
<td></td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>Not rested</td>
<td></td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Joint pain</td>
<td></td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>Joints stiff</td>
<td></td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Muscle pain</td>
<td></td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Body Pain</td>
<td></td>
<td>12%</td>
<td>5%</td>
</tr>
<tr>
<td>Headaches</td>
<td></td>
<td>17%</td>
<td>10%</td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>Light Sensitivity</td>
<td></td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Blurred vision</td>
<td></td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Numbness</td>
<td></td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Tremors</td>
<td></td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Temp Sensitivity</td>
<td></td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>Night Sweats</td>
<td></td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Scent Sensitivity</td>
<td></td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Rashes</td>
<td></td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Skin Problems</td>
<td></td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td></td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Breathing Trouble</td>
<td></td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>Coughing</td>
<td></td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Wheezing</td>
<td></td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Sore Throat</td>
<td></td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Sore Glands</td>
<td></td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Problems Concentrating</td>
<td></td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>Memory Problems</td>
<td></td>
<td>12%</td>
<td>8%</td>
</tr>
<tr>
<td>Speech Problems</td>
<td></td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>Irritability</td>
<td></td>
<td>15%</td>
<td>9%</td>
</tr>
<tr>
<td>Modiness</td>
<td></td>
<td>17%</td>
<td>7%</td>
</tr>
<tr>
<td>Anxiety</td>
<td></td>
<td>15%</td>
<td>7%</td>
</tr>
<tr>
<td>Sinus Problems</td>
<td></td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>Reduced Taste</td>
<td></td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Swallowing Problems</td>
<td></td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Hand-shoulder pain</td>
<td></td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>Back Problems</td>
<td></td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Digestive Problems</td>
<td></td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Gas</td>
<td></td>
<td>16%</td>
<td>9%</td>
</tr>
<tr>
<td>Arm or leg pain</td>
<td></td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Sickliness</td>
<td></td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Increased Sleeping</td>
<td></td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Weakness</td>
<td></td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Acknowledgements**

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  - John Evans
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