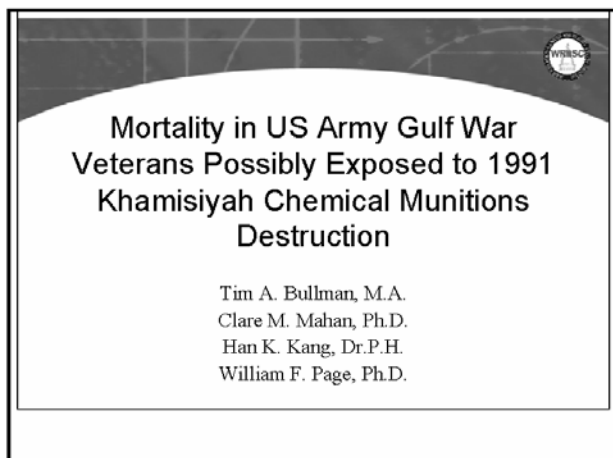


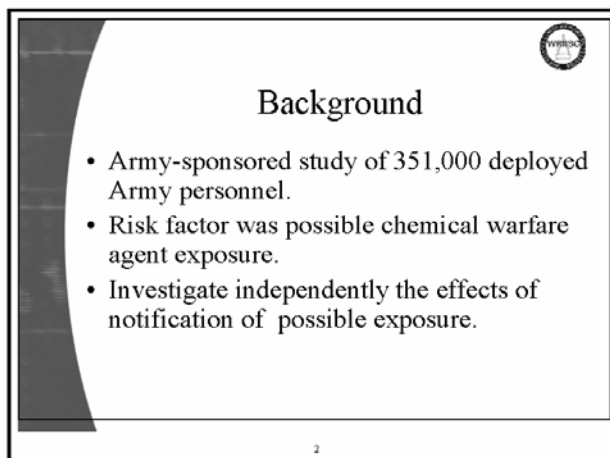
Presentation 13 – Tim Bullman



Mortality in US Army Gulf War Veterans Possibly Exposed to 1991 Khamisiyah Chemical Munitions Destruction

Tim A. Bullman, M.A.
Clare M. Mahan, Ph.D.
Han K. Kang, Dr.P.H.
William F. Page, Ph.D.

The slide features a dark header with a grid pattern and a circular logo in the top right corner. The main title is centered in a large, bold font. Below the title, the names of the four researchers are listed in a smaller font.

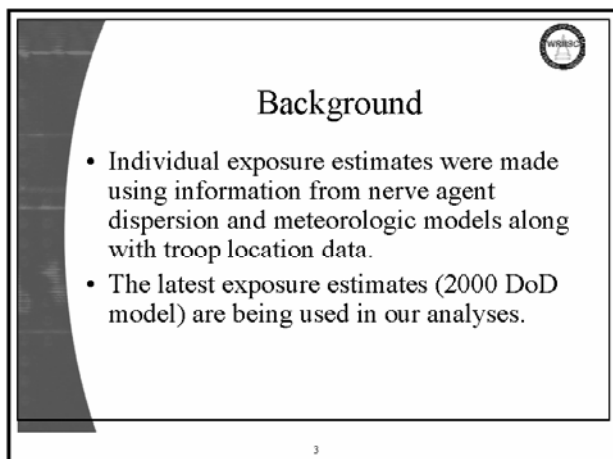


Background

- Army-sponsored study of 351,000 deployed Army personnel.
- Risk factor was possible chemical warfare agent exposure.
- Investigate independently the effects of notification of possible exposure.

2

The slide has a dark header with a circular logo in the top right corner. The title 'Background' is centered. Below it, three bullet points describe the study's scope and objectives. A small number '2' is centered at the bottom.

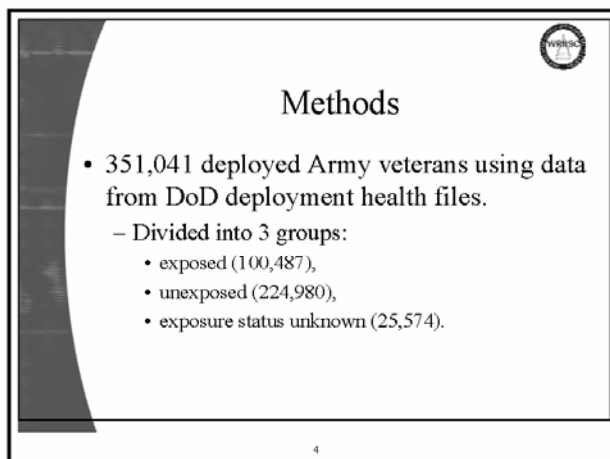


Background

- Individual exposure estimates were made using information from nerve agent dispersion and meteorologic models along with troop location data.
- The latest exposure estimates (2000 DoD model) are being used in our analyses.

3

The slide has a dark header with a circular logo in the top right corner. The title 'Background' is centered. Below it, two bullet points detail the methods used for exposure estimation. A small number '3' is centered at the bottom.



Methods

- 351,041 deployed Army veterans using data from DoD deployment health files.
 - Divided into 3 groups:
 - exposed (100,487),
 - unexposed (224,980),
 - exposure status unknown (25,574).

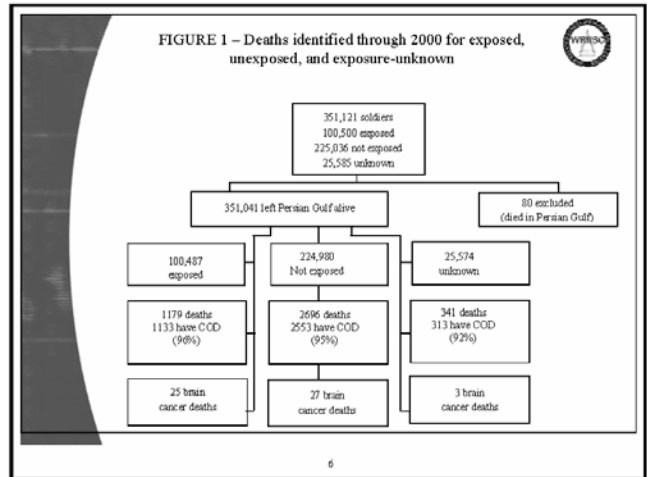
4

The slide has a dark header with a circular logo in the top right corner. The title 'Methods' is centered. Below it, a single bullet point describes the data source, followed by a sub-bullet point detailing the division of veterans into three groups. A small number '4' is centered at the bottom.

Methods

- **Vital status** was determined using VA and SSA records.
- **Cause of death** through December 31, 2000 came from National Death Index.
- For brain cancer deaths,
 - Hard copy death certificates and relevant medical records were obtained for additional review.

5



Methods

- **Demographic data** from Defense Manpower Data Center:
 - age, race, gender, rank, unit component, military occupational specialty, etc.
- **Further data** on the number of days in the hazard area (0, 1, 2, 3, 4) came from DoD Deployment Health.
- Smoke exposure data came from Army (CHPPM)

7

Methods

- **Crude death rates**
- **Unadjusted relative risk estimates**
- **Adjusted relative risk estimates derived from Cox Proportional Hazard Model.**

8

Methods

- **Covariates included**
 - Age,
 - Race (white, non-white),
 - Gender,
 - Rank (enlisted, officer, warrant officer),
 - Unit component (active duty, National Guard, reserves).

9

RESULTS

TABLE 1 – Khamsiyah, Iraq, 1991 Chemical Munitions Destruction Exposure Status for US Army Gulf War Veterans, by Selected Demographic and Service Characteristics

	All Exposed (n=100487)		All Unexposed (n=224900)		Exposure Unknown (n=25574)	
	#	%	#	%	#	%
Age in 1990						
≤ 31	23421	(23.3)	56509	(25.1)	4951	(19.4)
22-25	25825	(25.7)	58352	(26.2)	6795	(26.6)
26-31	24364	(24.2)	54982	(24.4)	6302	(24.6)
≥ 32	26877	(26.8)	54637	(24.3)	7526	(29.4)
Mean age in 1990 y	27.7		27.2		28.2	
Race						
White	65146	(64.8)	145009	(64.5)	16849	(65.9)
Non-White	35341	(35.2)	79971	(35.5)	8725	(34.1)
Gender						
Male	89777	(89.3)	204594	(90.9)	22225	(86.9)
Female	10710	(10.6)	20306	(9.1)	3349	(13.1)
Rank						
Enlisted	88802	(88.4)	202093	(89.8)	22161	(86.7)
Warrant Officer	1862	(1.8)	4728	(2.1)	703	(2.7)
Officer	9823	(9.8)	18159	(8.1)	2710	(10.6)
Unit Component						
Active	76464	(74.1)	175089	(77.8)	17745	(69.4)
Guard	11897	(11.8)	24445	(10.9)	1011	(3.9)
Reserve	14126	(14.1)	25466	(11.3)	6818	(26.7)

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RESULTS

# of days exposed	# Days Exposed	
	#	%
1	86167	85.7
2	12551	12.5
3	1657	1.7
4	112	0.1

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RESULTS

TABLE 2 – Cause-Specific Mortality Among Exposed US Army Gulf War Veterans at Khamsiyah, Iraq, in 1991 Compared With Unexposed Army Veterans

Underlying cause of death (ICD-9)	Exposed (n=100487) No. (Rate)	Not Exposed (n=224900) No. (Rate)	Relative Risks		
			Crude	Adjusted	95%CI
All causes	1179 (12.22)	2696 (12.47)	0.98	0.97	0.91, 1.04
All diseases (001-799)	496 (5.14)	1093 (5.05)	1.02	0.96	0.86, 1.07
Infectious and parasitic disease (001-139)	29 (0.30)	56 (0.26)	1.16	1.16	0.74, 1.82
Malignant neoplasm (140-208)	184 (1.91)	391 (1.81)	1.06	0.97	0.82, 1.16
Colon cancer (153)	14 (0.15)	26 (0.12)	1.25	1.17	0.61, 2.25
Lung cancer (162)	30 (0.31)	84 (0.39)	0.80	0.72	0.47, 1.10
Brain cancer (191-192)	25 (0.26)	27 (0.12)	2.17	1.94	1.12, 3.34
Disease of circulatory system (390-459)	170 (1.76)	407 (1.88)	0.94	0.89	0.74, 1.06
Disease of respiratory system (460-519)	22 (0.23)	45 (0.21)	1.10	1.03	0.62, 1.72
Disease of the digestive system (520-579)	34 (0.35)	46 (0.21)	1.17	1.10	0.67, 1.81
All external causes (E800-E989)	637 (6.60)	1460 (6.75)	0.98	1.01	0.92, 1.10

12

RESULTS

TABLE 2 – Cause-Specific Mortality Risk Among US Army Gulf War Veterans Exposed at Khamsiyah, Iraq, in 1991 Compared With Unexposed Army Gulf War Veterans

Underlying cause of death (ICD-9)	1 Day Exposure	≥ 2 Day Exposure	All Nonexposed	1-Day	≥ 2-Day
	(n=86167)	(n=14320)		(n=224980)	Exposure
	No. (Rate)	No. (Rate)	No. (Rate)	RR (95%CI)	RR (95%CI)
All causes	1020 (12.34)	159 (11.51)	2696 (12.47)	0.97 (0.90, 1.04)	0.96 (0.82, 1.13)
All diseases (001-799)	427 (5.17)	69 (5.00)	1093 (5.03)	0.95 (0.83, 1.06)	1.06 (0.83, 1.30)
Infectious and parasitic diseases (001-139)	24 (0.29)	5 (0.36)	56 (0.26)	1.11 (0.69, 1.80)	1.40 (0.59, 3.74)
Malignant neoplasms (140-208)	156 (1.89)	28 (2.03)	391 (1.81)	0.94 (0.78, 1.13)	1.25 (0.85, 1.84)
Brain cancer (191-192)	19 (0.23)	4 (0.43)	27 (0.12)	1.72 (0.95, 3.10)	3.26 (1.33, 7.96)

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RESULTS

Brain Cancer Deaths by Length of Exposure

# Days Exposed	# Deaths	Rate/100,000 Persons
0 Days	27	11.97
1 Day	19	22.05
2 Days	5	39.83
3 Days	1	60.35
4 Days	0	0.00

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RESULTS

Distribution Of Primary Cancer Cell¹ Type By Exposure Status For Brain Cancer Deaths

Cell Type ²	Exposure Status		
	Exposed (n=20)	Unexposed (n=21)	Unknown (n=2)
Astrocytoma	4	5	1
Glioblastoma	13	12	1
Glioma ²	2	2	
Oligodendroglioma	1	2	

¹Pathological classification for the balance of four confirmed primary tumors are not available. Richard Johnson, MD, Johns Hopkins University, who was blinded to exposure status, reviewed all available records to determine the type of primary brain cancer.

²Is a larger grouping of specific cell type

(An additional 3 were classified as primary brain tumors, but cell type not provided)


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Results

Exposure risk assessment using verified primary brain cancers

- Analysis of risk using only 44 confirmed primary brain cancer
- Exposed RR, 1.88 (1.04-3.41)
- Exposed 1 Day: RR=1.66
- Exposed 2 Days: RR=3.25

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Results

Risk of Brain cancer death by latency

- 1) Beginning of follow-up-1/31/94 (3 years) 6 exposed/7 unexposed. RR; 1.80, 95% C.I., 0.60-5.36.
- 2) 2/1/94-7/31/97. (6 years) 5 exposed/10 unexposed. RR; 0.99, 95% C.I., 0.34-2.91.
- 3) 8/1/97-12/31/00. (9 years) 14 exposed/10 unexposed. RR; 3.03, 95% C.I., 1.34-6.82


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Results

- For **exposure misclassification** to have affected the results, a minimum of three brain cancer deaths among the exposed would have to be reclassified as unexposed.
- Assigning all of veterans with **unknown exposure status** to either the exposed group or the unexposed group did not affect the results.


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Results

- **Modeled Oil Well Fire Smoke Data**
 - # days modeled exposure x average concentration of TSP
 - # days at TSP level of 0.260 mg/m³ or more x average concentration of TSP level for those days
 - the presence or absence of TSP exposure of 0.260 mg/m³ or greater
- Including each smoke exposure variable into model along with Khamisayah exposure, did not diminish risk of brain cancer death associated with Khamisayah exposure.

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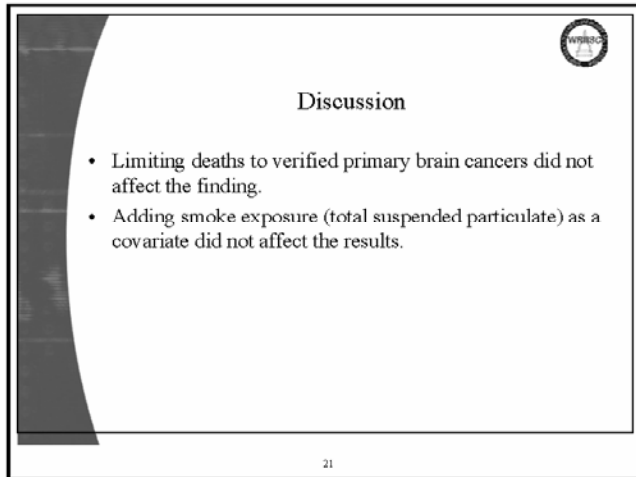


Discussion

- Only brain cancer mortality was significantly associated with possible chemical warfare agent exposure.
- There was a gradient of risk with number of days of possible exposure.
- Risk of brain cancer death increased as length of follow-up increased.

(Neither exposure misclassification nor missing exposure data could have easily accounted for this finding.)

20

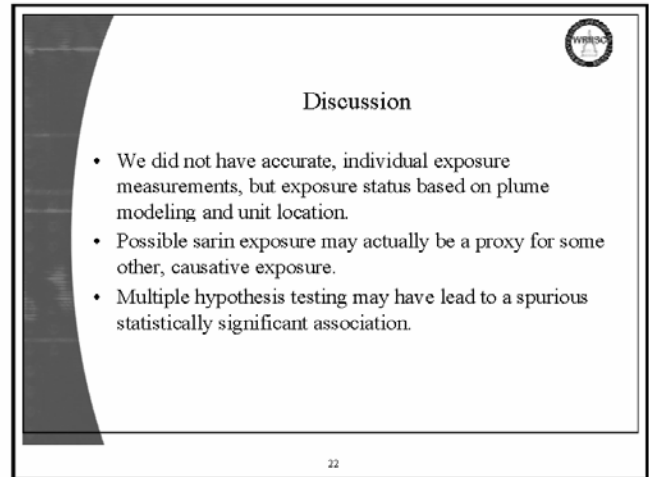


Slide 21 features a dark grey curved background on the left side and a circular logo in the top right corner. The title "Discussion" is centered at the top. Below it, two bullet points are listed. The slide number "21" is centered at the bottom.

Discussion

- Limiting deaths to verified primary brain cancers did not affect the finding.
- Adding smoke exposure (total suspended particulate) as a covariate did not affect the results.

21

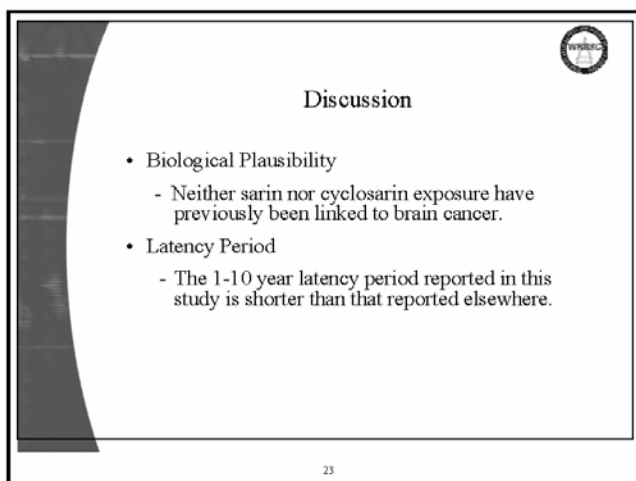


Slide 22 features a dark grey curved background on the left side and a circular logo in the top right corner. The title "Discussion" is centered at the top. Below it, three bullet points are listed. The slide number "22" is centered at the bottom.

Discussion

- We did not have accurate, individual exposure measurements, but exposure status based on plume modeling and unit location.
- Possible sarin exposure may actually be a proxy for some other, causative exposure.
- Multiple hypothesis testing may have lead to a spurious statistically significant association.

22

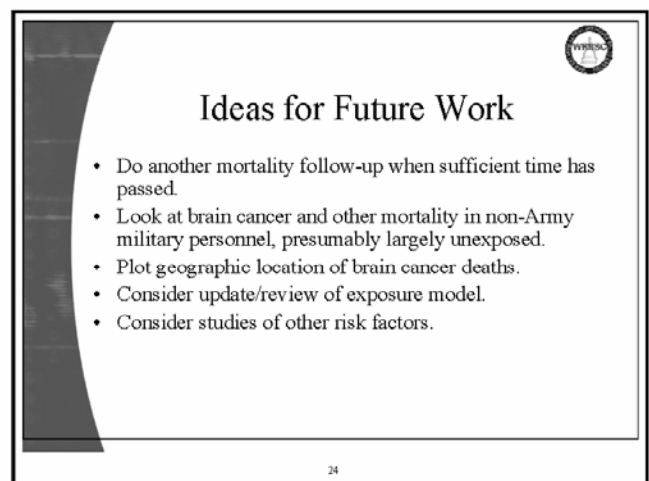


Slide 23 features a dark grey curved background on the left side and a circular logo in the top right corner. The title "Discussion" is centered at the top. Below it, two main bullet points are listed, with the second one having a sub-bullet. The slide number "23" is centered at the bottom.

Discussion

- Biological Plausibility
 - Neither sarin nor cyclosarin exposure have previously been linked to brain cancer.
- Latency Period
 - The 1-10 year latency period reported in this study is shorter than that reported elsewhere.

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Slide 24 features a dark grey curved background on the left side and a circular logo in the top right corner. The title "Ideas for Future Work" is centered at the top. Below it, five bullet points are listed. The slide number "24" is centered at the bottom.

Ideas for Future Work

- Do another mortality follow-up when sufficient time has passed.
- Look at brain cancer and other mortality in non-Army military personnel, presumably largely unexposed.
- Plot geographic location of brain cancer deaths.
- Consider update/review of exposure model.
- Consider studies of other risk factors.

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