

# “Overview of the Department of Veterans Affairs Surveillance and Research Activities in the Depleted Uranium and Embedded Fragment Cohorts”

*Melissa A. McDiarmid, MD, MPH, DABT  
Baltimore VA Medical Center  
University of Maryland, School of Medicine*



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# Historical Timeline of Fragment Related Events

1<sup>st</sup> DU  
Surveillance  
Cohort Visit

1<sup>st</sup> Gulf War



1991 1993



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## **Mission:**

- **Since 1993: To provide clinical surveillance for the ‘friendly fire’ DU-exposed GWI Veterans**
- **Since 1998: To provide biologic monitoring by mail to assess DU exposure for all GWI and OIF Veterans**

## Conducted at the Baltimore VA, the most recent evaluations included:

- Detailed history
- Physical examination
- Exposure assessment – Urine U concentrations
- Extensive laboratory studies (hematology, serum chemistry, neuroendocrine, urinalysis, renal markers, bone metabolism)
- Special imaging to survey for local effects
- Neurocognitive test battery
- Lung function tests

## Prior evaluations included:

- Semen analysis
- Skin patch testing for U hypersensitivity
- Whole body radiation counting
- Markers of genotoxic effect
- Chromosomal analysis
- Focus groups

**Sunsetted**



# Summary of 'Friendly-Fire' Surveillance Visits Through 2020

Visit Year	Gulf War 1		OIF	Total
	DU-exposed	Non-exposed	DU-exposed	
1993-4	33			33
1997	29	38		67
1999	21+29 new			50
2001	31+8 new			39
2003	32			32
2005	30+4 new		3	37
2007	32+3 new		2 (1 new)	37
2009	38+2 new		2	40
2011	36+1 new		2	39
2013	35			35
2015	36			36
2017	41+1 new			42
2019	36			36

81 Unique cases from have been evaluated from Gulf War 1

4 Unique cases from have been evaluated from OIF



# Why are fragments not removed?

Image provided by:  
Dr. Richard Breyer, Baltimore VAMC



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# Demographic Characteristics of the DU Surveillance 2019 Participants Compared to All Participants

	2019 Cohort (N=36)		All GW1 Participants (N=81)	
	N	(%) <sup>a</sup>	N	(%) <sup>a</sup>
<b>Race/Ethnicity</b>				
African American	11	(30)	24	(30)
Asian American	1	(3)	1	(1)
Caucasian	21	(58)	46	(56)
Hispanic	3	(8)	8	(10)
Native American	0	(0)	1	(1)
<b>Age<sup>b</sup></b>				
Mean	54		52	
s.d.	4.98		4.67	

<sup>a</sup> May not add to 100% due to rounding

<sup>b</sup> Age at 2019 visit

# Mean uU Concentrations Across 13 visits by 2019 Surveillance Visit Participation

	<u>2019 DU</u> <u>Cohort</u>	<u>Rest of DU</u> <u>Cohort</u> <u>(did not attend</u> <u>in 2019)</u>	<u>Mann</u> <u>Whitney</u> <u>p</u>
<b>Low uU</b> <b>group*</b>	Mean 0.031 SE 0.011 N 26	Mean 0.019 SE 0.004 N 40	0.813
<b>High uU</b> <b>group**</b>	Mean 7.900 SE 3.690 N 10	Mean 4.650 SE 2.582 N 5	0.440

\* Urine U <0.10 mcg/g creatinine during most recent visit

\*\*Urine U ≥0.10 mcg/g creatinine during most recent visit



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## CLINICAL FINDINGS

- Sustained elevated urine U excretion seen in Veterans with DU fragments >20 years after time of injury
- No clinically significant differences detected between low and high U exposure groups for:
  - Hematology parameters
  - Urine chemistry parameters
  - Semen characteristics
  - Neuroendocrine measures
  - Neurocognitive measures

- But signals for proximal tubule effects and abnormal bone mineral density as a function of U level.
- On-going accrual of U, co-morbidities and aging of the cohort recommend continued surveillance.





# Historical Timeline of Fragment Related Events

1<sup>st</sup> DU  
Surveillance  
Cohort Visit

Mail-in  
biomonitoring  
for DU  
Exposure

1<sup>st</sup> Gulf War



1991

1993

1998



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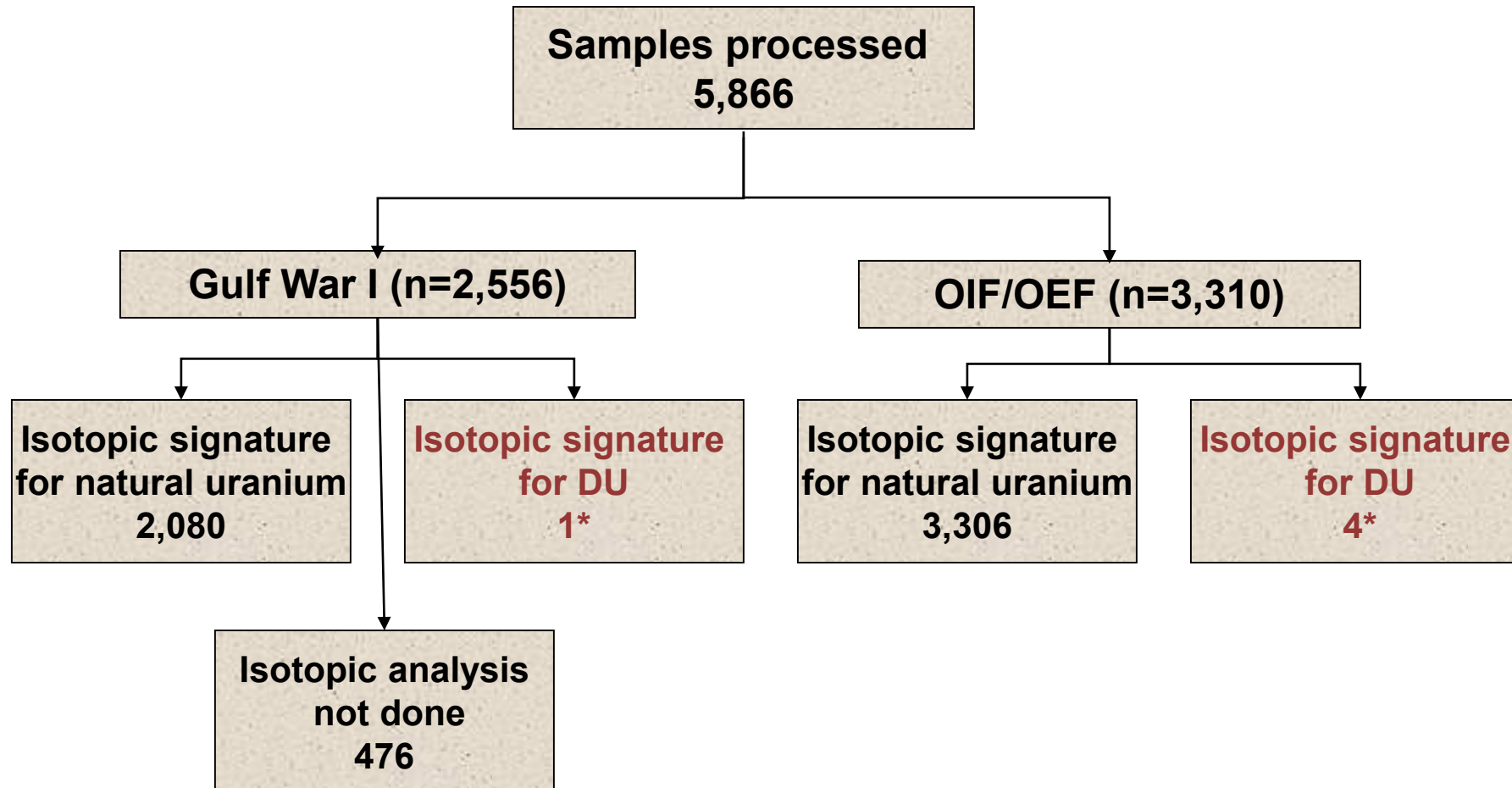


## PURPOSE OF THE DU URINE BIOMONITORING PROGRAM

- Determine urine uranium concentrations in any Veteran who requests testing
- Perform passive surveillance for exposure scenarios linked to DU exposure other than friendly fire
- Provide assistance to Veterans' primary care providers in interpreting results and answering Veterans questions



# RESULTS OF DU URINE SURVEILLANCE (AS OF DECEMBER 31 2018)



**\*All with DU signature were invited to enter the DU Follow-up Program.  
Three from OIF/OEF declined but may be interested in future follow-up.**



# Historical Timeline of Fragment Related Events

1<sup>st</sup> DU  
Surveillance  
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Mail-in  
biomonitoring  
for DU  
Exposure

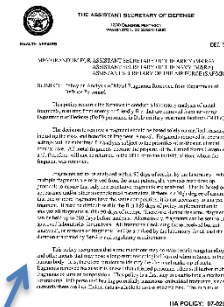
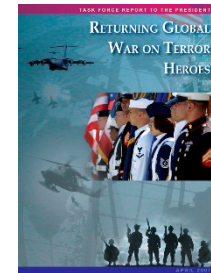
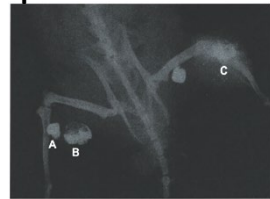
Hahn et al  
article  
published

VHA directed to establish  
surveillance program &  
registry

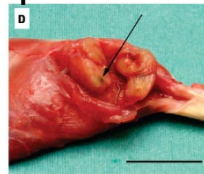
DoD Fragment  
Analysis Policy

Establishment  
of VA Toxic  
Embedded  
Fragment  
Surveillance  
Center  
(TEFSC)

1<sup>st</sup> Gulf War



Kalinich et  
al article  
published



Iraq War



1991 1993

1998 2001 2002

2005 2007 2008

# Background

- Traumatic injuries via contact with improvised explosive devices (IEDs) are a “signature injury” for those who served in Iraq and/or Afghanistan.
  - More than 44,000 Veterans may have embedded fragments; many from Improvised Explosive Devices (IEDs)
  - IEDs are packed with heterogeneous material that may lead to local and systemic adverse health effects

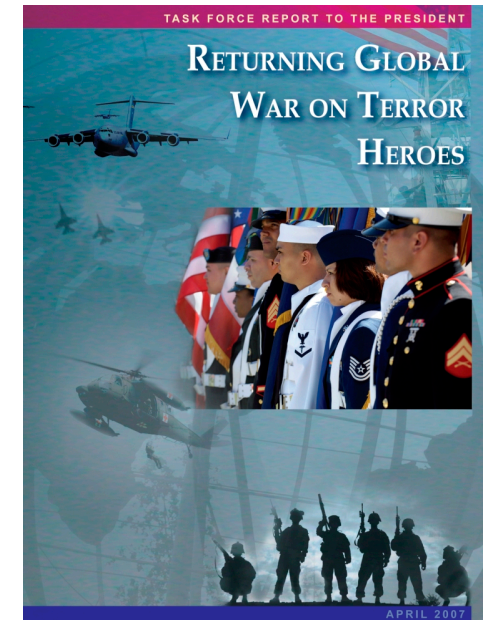


Photos: wikipedia





- 2008: Established to provide care and active medical surveillance for Veterans with retained embedded fragments
- Concerns:
  - Local effects: risk of developing tumors at fragment sites
  - Systemic effects: risk of target organ effects arising from chemicals released from fragments



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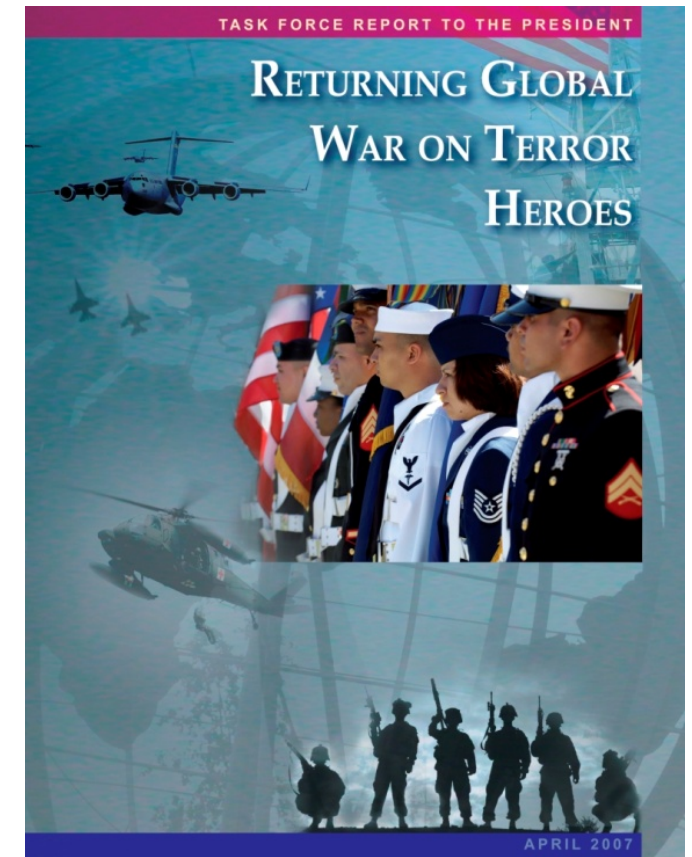
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# Toxic Embedded Fragment Surveillance Center

- **Mission:** To track, monitor, provide follow-up care and active medical surveillance for Veterans with embedded fragments
- **Functions of the TEFSC:**
  - Registry development
  - Fragment Characterization
  - Biomonitoring & Medical Surveillance
  - Clinical Consultation



April 2007



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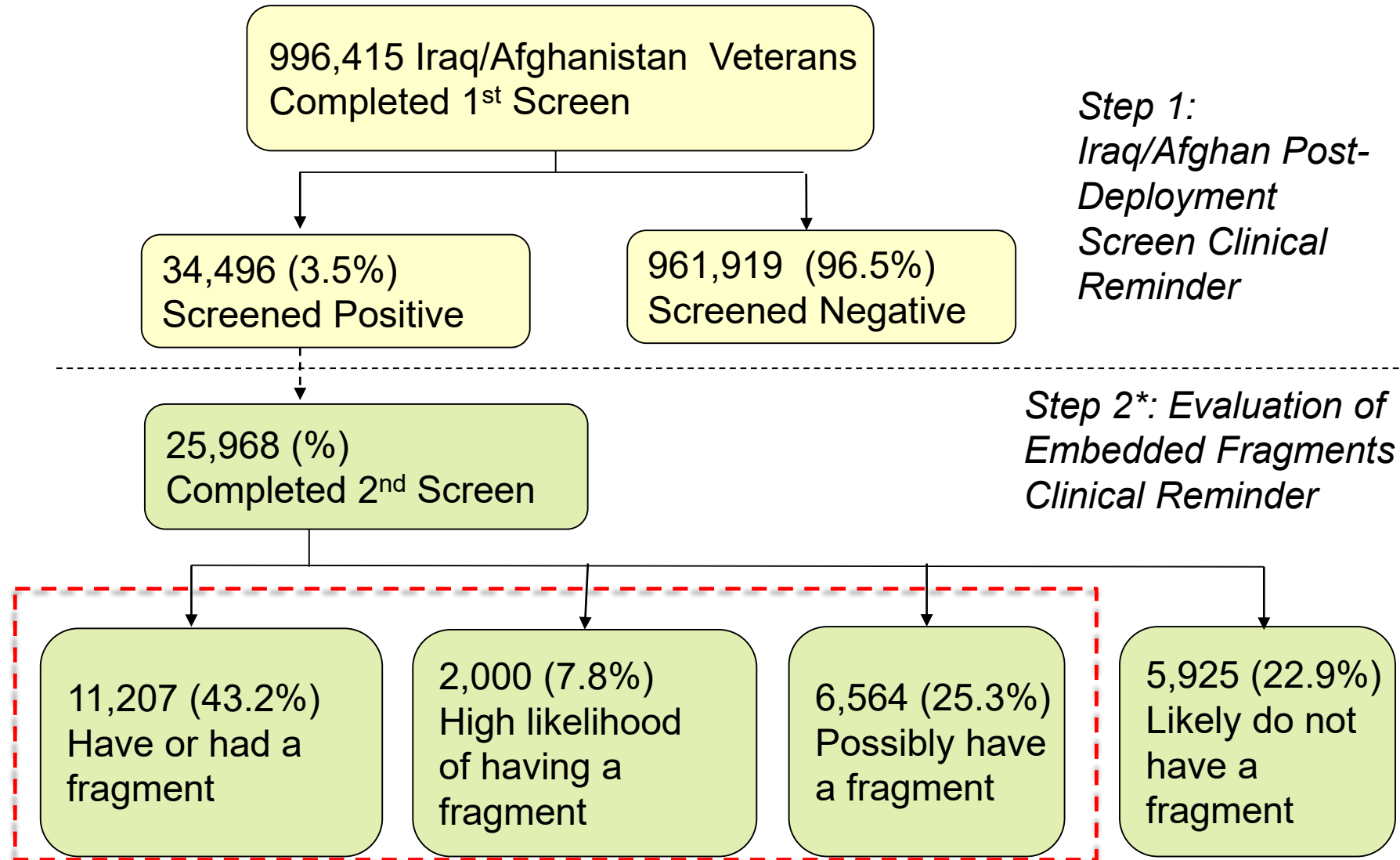
# VA's Embedded Fragment Registry

- **Eligible Veterans:**
  - Served in Iraq and/or Afghanistan
  - Have or likely have a retained fragment from an injury received while serving in the area of conflict
  - Identified using a series of screening questions
- Almost 17,000 Veterans currently enrolled





# SCREENING RESULTS AS OF DECEMBER 31 2018



**\*\*Completion of the 2<sup>nd</sup> clinical reminder triggers inclusion in the Embedded Fragment Registry.**

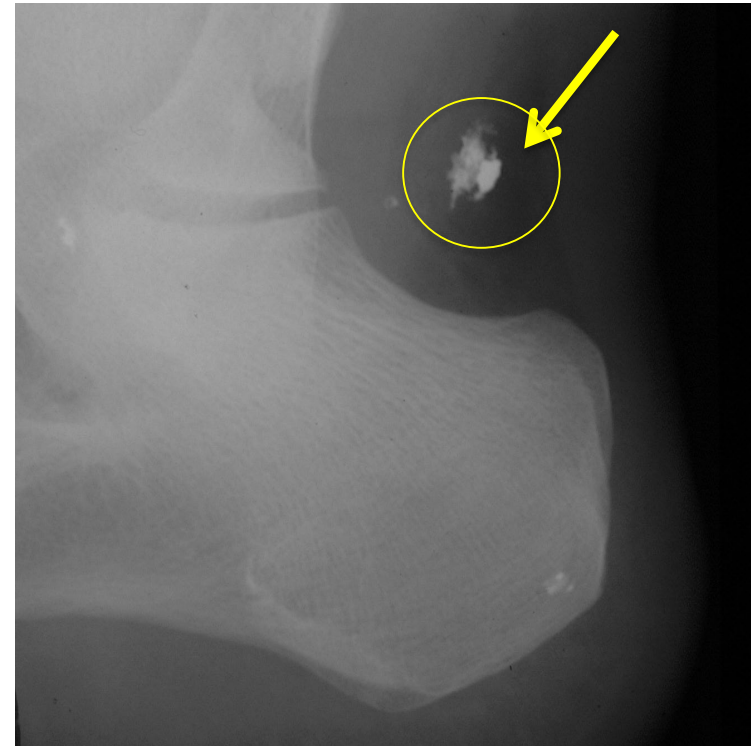
# Surveillance Protocol for Veterans with Embedded Fragments

- Characterization of removed fragments
- **Urine biomonitoring** via mail
- Imaging surveillance of embedded fragment location and shape
- Target organ surveillance for toxicants of concern





**1995 film**



**2001 film**

Change in DU fragment appearance over time;  
suggests oxidation in situ and additional imaging is  
warranted.



# Urine Biomonitoring

- Spot urine collection to measure concentrations of 14 metals
- Specimens and exposure questionnaires mailed to Baltimore VA
- Metal analyses conducted by the Joint Pathology Center
- Interpretation letters provided to Veteran and VA provider

## Toxicants of Interest

- Aluminum (Al)
- Arsenic (As)
- Cadmium (Cd)
- Chromium (Cr)
- Cobalt (Co)
- Copper (Cu)
- Iron (Fe)
- Manganese (Mn)
- Molybdenum (Mo)
- Nickel (Ni)
- Lead (Pb)
- Uranium (U)
- Tungsten (W)
- Zinc (Zn)



# Systemic Exposure from Retained Metal in other Populations

- Elevated blood lead levels (BLLs) documented in gunshot victims who have retained bullets.

(Dillman et al., 1979; Bustamante et al., 2016; McQuirter et al., 2001, 2004, Mago 1999)

- Sustained urine uranium concentrations in Veterans with retained depleted uranium (DU) fragments. (McDiarmid et al., 2015, 2017)

- Elevated concentrations of cobalt and chromium in metal-on-metal hip implant patients.





# Interpretation of Urine Biomonitoring Results

Metal	Ref. Value (ug/g cre)	Level of "Concern"	Additional Notes
Al	30 <sup>a</sup>	150 ug/g cre	Based on neurobehavioral outcomes <sup>a</sup>
As	53.90 <sup>b</sup>	35 ug/L	BEI for Inorganic As
Cd	1.02 <sup>b</sup>	3ug/g cre	OSHA Action Level based on renal damage
Cr	2.0 <sup>c</sup>	25ug/L	BEI for Cr(VI) based on respiratory outcomes
Co	0.98 <sup>b</sup>	15 ug/L	BEI based on respiratory outcomes
Cu	50 <sup>d</sup>	>60 mcg/L	Concerns of Wilsons Disease
Fe	300 <sup>d</sup>	-	
Pb	1.94 <sup>b</sup>	-	Obtain BLL if urine elevated
Mn	2 <sup>e</sup>	-	1-8ug/L in general population (ATSDR/CDC)
Mo	127 <sup>b</sup>	-	
Ni	10 <sup>c</sup>	10ug/L	Based on renal effects (FDA, unpublished)
W	0.28 <sup>b</sup>	-	0.48-1.19 ug/L in drinking H2O exposed pop (ATSDR/CDC) 10.6-168.6ug/g cre in healthy W-exposed workers (Kraus et al, 2001)
U	0.03 <sup>b</sup>	-	70 ug/g cre reported in DU-exposed cohort (McDiarmid et al 2015,2017)
Zn	1300 <sup>e</sup>	-	

## Key Points:

- Prefer to use NHANES data to establish reference values
- Levels linked to health effects are often based on different exposure pathways

# Interpretation of urine biomonitoring results

## What if results are above reference value?

- Consider other sources of exposure

- Occupation
- Hobbies
- Metal implants
- Supplements
- Piercings
- Tattoos
- Diet



- Consider additional testing

- BLLs if urine Pb is elevated
- Speciation testing to determine if As is inorganic vs. organic

- Recommend repeat urine biomonitoring

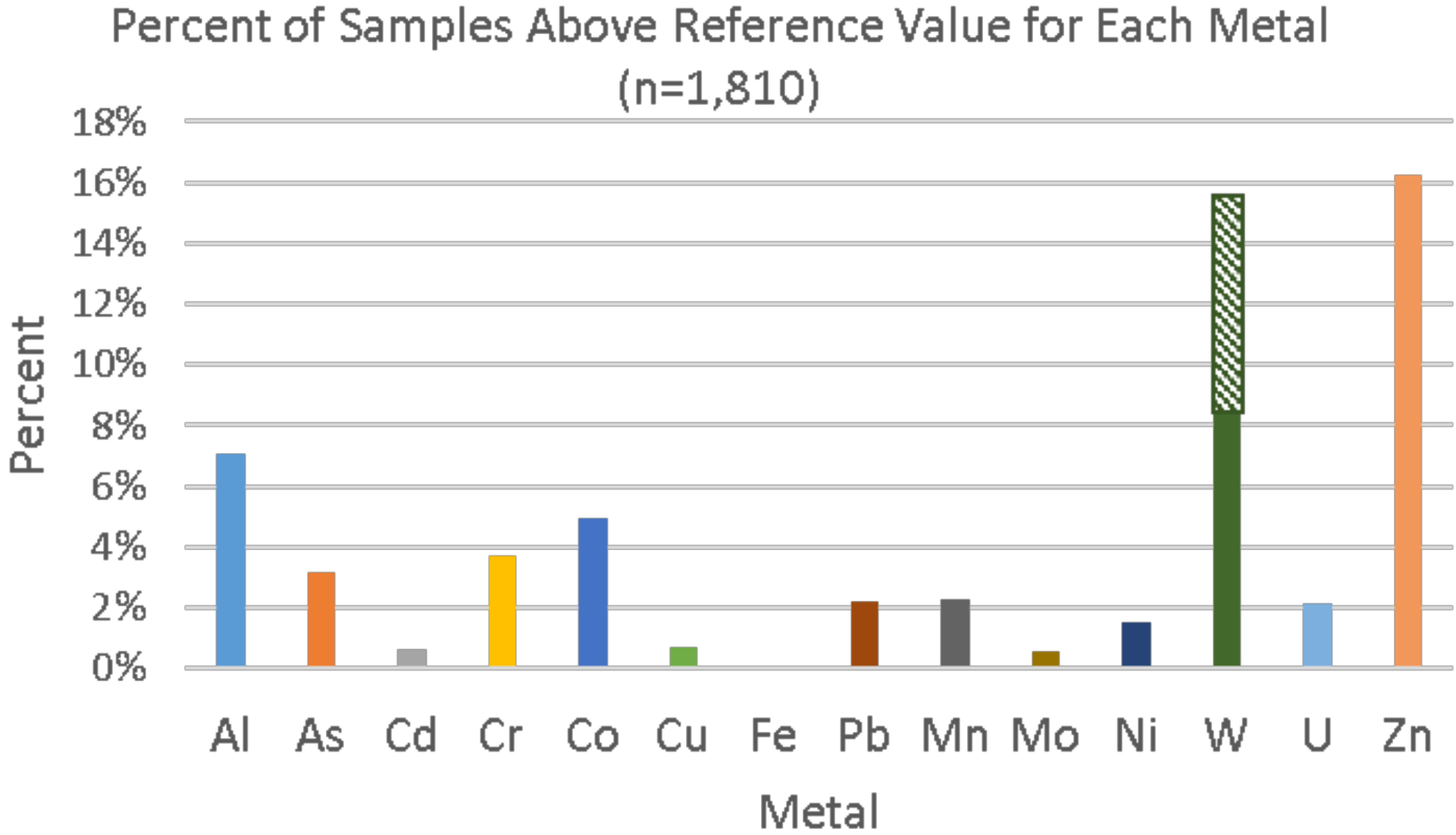
- Values are compared to:
  - Our reference values
  - Levels linked to health effects
  - Distribution of results

<b>Recommended timeframe for obtaining another urine sample</b>	<b>If...</b>
5 years	All values are below are reference values
2 years	“Slightly above” reference values
3-6 months	Above reference values but below a level linked to health effects
Repeat now	At or above a level linked to health effects





- Majority of samples (~60%) have no metal elevations.



# SUMMARY OF TEF PROGRAM KEY POINTS

- Embedded fragments pose **potential local and systemic health effects**.
- Current VA efforts assist in:
  - Identifying the **at-risk population**
  - Characterizing **systemic metal exposure** related to retained fragments
  - Anticipating **potential health effects**
  - **Optimizing** the **care** provided to affected Veterans
- Major findings to date:
  - Majority of urine results all within established reference ranges and will serve as a baseline for future follow-up
  - To date, no recommendation has been made to remove a fragment based on metal elevation



# Conclusion

**Urine biomonitoring, performed at intervals over the long-term, is a non-invasive method to help better identify and characterize fragment-related exposures and associated systemic metal body burden.**



# QUESTIONS?



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