Dr. Kimberly Sullivan requested the following updates from OPH on behalf of the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC) in a March 4, 2014 email to Dr Victoria Davey, Chief Public Health Officer:

1) The cause specific mortality data results in GW veterans
2) The National Survey of Gulf War Veterans results to date
3) The 2005 national survey results regarding the 'treatments tried' questions.
4) How many Gulf War veterans are also included in New Generation survey cohort and if it would be possible for that dataset to be used to study GW veterans as well.

This document will provide responses to these inquiries. This information is intended to accompany the scheduled OPH presentations at the RAC meeting on April 28, 2014.

1) **The cause specific mortality data results in GW veterans**

- A cohort consisting of 621,901 Gulf War Veterans who served in the Persian Gulf during the time of armed conflict from August 1, 1990 – March 1, 1991 and 746,248 control group Veterans who served during the Gulf War but were not deployed to theater were matched to mortality data obtained from the Centers for Disease Control and Prevention (National Death Index).
- Follow-up of death for deployed Gulf War Veterans began the year they left theater and May 1, 1991 for non-deployed Gulf War Veterans.
- Follow-up ended at date of death or December 31, 2011
- Data were analyzed using the CDC National Institute for Occupational Safety and Health Life Table Analysis System (LTAS)

Leading causes of death, Deployed and Non-Deployed Gulf War Veterans, 1991-2011

Deployed Gulf War Veterans, total deaths n=21,144 (total n= 621,901)

1. Malignant neoplasms n=4594
2. Heart diseases n=3499
3. Transportation injuries n=2969
4. Intentional self-harm n=2471
5. Other injury (major) n=1484
6. Other and unspecified causes n= 1054
7. Assault and homicide n=906
8. Other diseases of the circulatory system n=891
9. Diseases of the digestive system n=818
10. Diseases of the respiratory system n=539

Non-Deployed Gulf War Era Veterans total deaths n=29,340; total n= 746,247

1. Malignant neoplasms n=7603
2. Heart diseases n=5227
3. Transportation injuries n=3038
4. Intentional self-harm n=2831

5. Other injury (major) n=1754
6. Other diseases of the circulatory system n=1392
7. Other and unspecified causes n= 1308
8. Diseases of the digestive system n=1153
9. Assault and homicide n=980
10. Diseases of the respiratory system n=942

Specific causes of death of interest among Deployed and Non-Deployed Gulf War Veterans

Deployed Gulf War Veterans total deaths n=21,144; total n= 621,901

- Malignant neoplasm (trachea, bronchus, lung), n= 1082, SMR= 0.60, 95% CI= 0.57, 0.64
- Multiple sclerosis, n=31, SMR= 0.47, 95% CI= 0.32, 0.66
- Malignant neoplasm (brain & other nervous), n= 307, SMR= 0.88, 95% CI=0.78, 0.98
- Intentional self-harm, n=2471, SMR= 0.91, 95% CI= 0.88, 0.95
- Motor vehicle (driver), n= 1237, SMR= 0.97, 95% CI= 0.91, 1.02

Non-Deployed Gulf War Era Veterans total deaths n=29,340; total n= 746,247

- Malignant neoplasm (trachea, bronchus, lung), n= 1868, SMR= 0.59, 95% CI= 0.56, 0.62
- Multiple sclerosis, n=49, SMR= 0.48, 95% CI= 0.36, 0.64
- Malignant (neoplasm brain & other nervous), n= 462, SMR= 0.93, 95% CI=0.85, 1.02
- Intentional self-harm ,n=2831, SMR= 0.91, 95% CI= 0.88, 0.95
- Motor vehicle – driver, n= 1247, SMR= 0.88, 95% CI= 0.83, 0.93

2) **The National Survey of Gulf War Veterans results to date**

- The study has now surveyed the sample of 15,000 deployed and 15,000 non-deployed three times: 1993-1995; 2003-2005 and 2012-2013
- The survey used a multimodal survey methodology using paper-and-pencil, web-based, and telephonic data collection. This was the first use of web-based survey methods with this Gulf war panel.
- Survey responses were overall approximately 50%. Approximately two-thirds responded by postal survey (~68%), about one-quarter (26%) by web and the remainder were interviewed by telephone.
- Responses were comparable across mode by most demographic variables. More detailed analyses of response patterns will follow. See presentation slide for table of preliminary results.
- Limited analyses on neurological disease were prepared for the RAC presentation. These are preliminary crude prevalence rates. For the survey sample they are self-reported disease based on the following question: "Has a doctor ever told you that you have any of the following conditions?" that precedes a list of 33 response options. The following table presents a limited number of neurological findings that OPH felt would be of interest to the RAC. The columns to the right of the table present GW era health care utilization as a comparison. The comparison is based on a matching procedure with the VHA health care utilization files for Fiscal year 2013 and the GW deployed file provided to OPH by DoD (n=621,901 who served between Aug 1990

2

through February 1991) and a comparison file of nondeployed (n=746,247 or a 50% sample of the nondeployed GW era Veterans).

Table: Crude prevalence estimates of selected neurological diseases based on self-reported survey data from the 2013 Follow-up Study of Gulf War and Gulf Era Veterans and fiscal year 2013 health care utilization for Gulf War deployed and Gulf War era Veterans seen at VHA facilities.

Condition	GW Follow-up Study		Gulf Era VHA Utilization FY13	
	Deployed (N=7,992)	Non-deployed (N=5,660)	Deployed** (N=185,741)	Non-Deployed*** (N=168,747)
Unexplained multisymptom illness	44.5%	18.4%	*	*
Multiple Sclerosis	0.73%	0.61%	0.40%	0.44%
Chronic Fatigue Syndrome	13.4%	4.5%	0.45%	0.12%
Fibromyalgia	5.4%	3.12%	2.9%	2.2%
Irritable Bowel Syndrome	15.1%	9.3%	2.0%	1.09%
Migraines	21.3%	14.8%	*	*
Migraine/Headache	*	*	4.9%	4.7%
Brain Cancer	0.40%	0.24%	0.18%	0.20%
Parkinsons' Disease	0.72%	0.60%	0.17%	0.22%

- The Sub-Study of Veterans Expressing Suicide Ideation extended the routine practice standard in research of providing information about how to reach the Veterans Crisis Line (VCL) to active outreach to Veterans who may be at risk.
  - Followed up with every response to the following item on Patient Health Questionnaire 9 item screener for depression (PHQ9): Over the past 2 weeks how often have you been bothered by any of the following problems: "Thoughts that you would be better off dead or hurting yourself." Response choices: Not at all; Several days; More than half the days; or Nearly every day. Any response other than Not at all was referred for outreach.
  - Outreach team coordinated by WRIISC at DC VAMC; consisted of psychologists and social workers.
  - Over 1,500 calls; over 1150 contacts;
  - Approximately 3.6% (n=56) directly transferred to VCL.
  - Crisis Line phone number, connection to local resources including Vet Centers, education about mental health diagnoses and treatment options
  - Detailed follow-up for some cases included assistance with eligibility, introduction to Rural Treatment Coordinator or Seamless Transition Office
  - Crisis Line phone number, connection to local resources including Vet Centers, education about mental health diagnoses and treatment options

- o Detailed follow-up for some cases included assistance with eligibility, introduction to Rural Treatment Coordinator or Seamless Transition Office
- o Crisis Line phone number, connection to local resources including Vet Centers, education about mental health diagnoses and treatment options
- o Detailed follow-up for some cases included assistance with eligibility, introduction to Rural Treatment Coordinator or Seamless Transition Office

- Future analyses will evaluate comparisons between deployed and nondeployed. The following list is a selection of the topic areas preliminarily scheduled:
  - o Prevalence of health conditions and health states
  - o Prevalence of multisymptom illness and presumptive conditions
  - o Prevalence of neurologic conditions & relationship to chronic multisymptom illness
  - o Longitudinal analyses of self-reported exposures and the development of chronic multisymptom illness and other presumptive conditions
  - o Development and persistence of disease
  - o Assessment of mortality: all cause and specific causes
  - o Comparison of health status/ functional health measures between Gulf War era and New Generation (OEF/OIF) cohort

3) The 2005 national survey results regarding the 'treatments tried' questions.

The 2005 survey included items regarding treatments for completion by individuals with unexplained multisymptom illness. The items were included at the request of the RAC, in close consultation with Dr. Lea Steele. Preliminary analysis results of the data will be shared here.

Background
- Questions
  - – Activities that made illness better or worse
  - – Treatments that made symptoms better or worse
  - – Treatments that did not have any effect on symptoms
- Unexplained Multisymptom Illness (MSI) defined as
  - – Several different symptoms together that persist for 6 months or longer
  - – Not adequately diagnosed by conventional medical or psychiatric diagnoses
  - – May be diagnosed as chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, or multiple chemical sensitivity
- **Results show wellness model is best approach to treatment**
  - – PACT model of multidiscplinary care responds to this need
  - – Findings have supported introduction of CAM practices and other treatments at WRIISCs and sites across the system
  - – Research projects on CAM practices supported by ORD and CDMRP

Results Overview
- Made MSI symptoms worse:
  - – Exercise, smoking, drinking and maintaining a busy schedule
- Made symptoms better:
  - – Maintaining balanced diet, regular sleep, cutting back on work/social activities, and avoiding stressful situations and exposure to certain chemicals/smells

- Asked if the condition was improving or getting worse, respondents with MSI answered with the following

	GW deployed	GW Non-deployed
Getting better	24%	41%
About the same	36%	28%
Getting worse	40%	31%

Treatment Findings
- Prescription drugs and OTC drugs are by far the most common treatments that were used for MSI symptoms
- Other category (in descending order): treatment by mental health providers, relaxation therapy, herbal medicine, sleep study, and massage, were most common
- Most frequently reported symptoms helped by above treatments included:
    - headache
    - joint/muscle pain
    - fatigue
    - depression and anxiety
    - sleep difficulty

Treatment Analyses
- The following table shows the number and percentage of respondents who reported the presence of multisymptom illness for 6 months or longer. This is the findings that established a 25% excess of multisymptom illness (MSI) complaints among the deployed

Table. Number and Percentage with
Mulitsymptom Illness 6 months or longer

	Gulf (N=5767)	Gulf-era (n=3459)
	N (%)	N (%)
No	3751 (65)	3104 (90)
Yes	2016 (35)	355 (10)

The tables below display the demographic and military characteristics of the respondents with MSI by deployment status.

Table. Demographic Characteristics for 2005 Gulf War Survey

Demographics	Gulf MSI %		Gulf-era MSI %	
	Yes	No	Yes	No
Gender				
Male	75	82	69	78
Female	25	18	31	22
Race				
White	70	80	77	82
Black	21	14	17	12
Hispanic	6	3	3	3
Other	3	3	3	3
Marital Status				
Married	56	55	60	62
Single	38	40	31	33
Other	6	5	9	5
Median Age (1991)	30	29	33	33

Table. Military Characteristics for 2005 Gulf War Survey

Military Charachteristics	Gulf MSI %		Gulf-era MSI %	
	Yes	No	Yes	No
Rank				
Enlisted	88	81	82	75
Officer	12	19	18	25
Branch				
Air Force	9	15	13	13
Army	73	59	68	65
Marine	9	11	8	9
Navy	9	15	11	13
Component				
Active	34	38	40	39
Guard	32	27	26	27
Reserve	34	35	34	34

The table below shows the distribution by year that Veterans responding to the survey first experienced unexplained MSI. It appears that the majority, regardless of deployment status, first

experienced symptoms, during the first two years of the period of observation. First reported symptoms fell off more rapidly for deployed.

Table. Year of first presentation of Multisymptom Illness by deployment status

Year	Gulf	Gulf-era
1991-1993	67.2	41.4
1994-1996	15.0	19.6
1997-1999	8.7	18.2
2000-2002	7.3	16.9
2003-2005	1.9	3.9
Median Year	1992	1995

The activities in the following table, when employed, had either no effect or a deleterious effect on symptoms.

Table. Effect of Activities on Gulf War Veterans Unexplained Symptoms

Activity	Worse	No Effect	Better	Not Sure	Not Tried	B/W*
Light Exercise	19.7	38.1	11.9	24.7	5.4	0.6
Vigorous exercise	36.6	21.9	8.0	19.8	13.5	0.2
Smoking tobacco	5.3	21.3	2.0	16.0	55.1	0.4
Drinking alcohol	7.6	28.9	6.5	22.2	34.6	0.9
Maintaining a busy work or social schedule	24.5	38.6	5.1	24.2	7.4	0.2

*Better/Worse

The activities in the following table, when employed, had either no effect or a salutary effect on Veterans' symptoms.

Table. Effect of Activities on Gulf War Veterans Unexplained Symptoms

Activity	Worse	No Effect	Better	Not Sure	Not Tried	B/W*
Maintaining a generally well balance diet	2.2	36.9	20.4	29.4	10.9	9.1
Adopting specific eating	2.5	29.9	17.8	23.3	26.3	7.1
Maintaining a regular sleep schedule	4.0	42.0	14.7	23.5	15.7	3.7
Cutting back on work or Social activities	5.2	34.3	18.3	22.5	19.5	3.5
Avoiding stressful situations	2.9	30.4	25.1	25.9	15.4	8.4
Avoiding exposure to certain chemicals or smells	3.4	23.0	13.6	28.7	31.0	3.9

*Better/Worse

Prescription and over the counter drugs were used most widely by survey respondents and were perceived to be helpful for treating symptoms.

Table. Treatments Veterans have used and for symptoms and number who reporting effect.

Treatments	Helped (n)	Made Worse (n)	Ratio**
Prescription Drug	889	175	5.1
Over the Counter Drug	546	62	8.8
Others*	412	135	3.1
Physical Therapy, Surgery	262	85	3.1
Nutrition Supplement And Dieting	207	35	5.9

*Includes acupuncture, massage, meditation, prayer, relaxation therapy, illegal drug use,
      cognitive therapy, counseling, interpersonal skills, sleep management, psychotherapy
** Ratio of number of veterans helped/the number of veterans whose symptoms got worse

The table below shows the number and percent reporting specific treatments used for unexplained symptoms. This describes in greater detail the categories of pharmacotherapy counted in the table above, as well as quantifying use of exercise, physical therapy, and dietary interventions.

Table. Top ten treatments that helped Gulf War Veterans' unexplained symptoms

Treatments	Number	Percent
Generic OTC Medication	181	7.8
Dieting and Nutritional Supplements	175	7.6
Physical Therapy	138	6.0
OTC non-opioid analgesics	131	5.7
Rx antidepressants	126	5.4
OTC non-opioid anti-inflammatories	93	4.0
Rx anti-inflammatory agents	88	3.8
Rx non-opioid analgesics	79	3.4
Physical exercise	69	3.0
Rx stomach blockers	62	2.7

Although the number reporting different treatment modalities is modest, it shows that both traditional therapy and some alternative practices were popular among respondents. Notable is that relaxation therapy, meditation and yoga, and acupuncture are alternative practices offered at the War Related Illness and Injury Study Centers.

Table. List of "other" treatments reported and the number and percentage reporting.

Treatments	Number	Percent
Acupuncture	5	0.2
Magnets, polarity therapy	6	0.3
Massage	26	1.1
Breathing exercises	10	0.4
Mediation, yoga	10	0.4
Relaxation therapy	50	2.1
Herbal medicine	40	1.7
Illegal drug use	13	0.6
Mental health (counseling, psychologist, Psychiatrist)	50	2.1
Radiation therapy	8	0.4
Interpersonal relationship skills	11	0.5
Sleep study	32	1.4

The following two tables describe the most frequently used therapies and practices and how effectively they addressed different symptoms. Pain and fatigue were dominant among the symptoms that were relieved across all intervention modalities.

Table. Effectiveness of selected treatments reported by Gulf War Veterans, duration of improvement, and the symptoms helped.

Treatment	N	Improvement, %		Affected Symptoms, %		Top 3 Symptoms Helped
		Short	Long Term	All	Some	
Generic OTC medication	181	72	28	12	88	headache, joint pain, depression
Dieting and Nutritional Supplements	175	53	47	10	90	fatigue, joint pain, IBS
Physical therapy	138	90	10	5	95	joint pain, back pain, muscle pain
OTC non-opioid analgesics	131	91	9	8	92	headache, joint pain, muscle pain
Rx antidepressants	126	52	48	6	94	depression, anxiety, sleep difficulty

Table. Effectiveness of selected alternative practices reported by Gulf War Veterans, duration of improvement, and the symptoms helped.

Treatment	N	Improvement, %		Affected Symptoms, %		Top 3 Symptoms Helped
		Short	Long Term	All	Some	
Massage	26	80	20	20	80	muscle pain, joint pain, back pain
Meditation, Yoga, Prayer	10	60	40	22	78	anxiety, headache, muscle pain
Relaxation Therapy	50	84	16	15	85	joint pain, fatigue, headache
Herbal Medicine	40	69	31	11	89	memory loss, fatigue, joint pain
Sleep Study	32	69	31	13	87	fatigue, headache, sleep difficulty

4) **How many Gulf War veterans are also included in New Generation survey cohort and if it would be possible for that dataset to be used to study GW veterans as well**

- New Generation (NewGen) panel members with Gulf War service. These are individuals who were sampled for the New Generation study and were found to have been present in the file of Gulf War deployed or the Gulf War non deployed.
  - o 3,049 Gulf War Veterans in the NewGen Panel
  - o 3,329 Gulf-era Veterans in the NewGen Panel

- New Generation respondents with Gulf War Service. These Veterans are a subset of the numbers above who were sampled and returned a New Generation study survey.
  - o 1,466 Gulf War Veterans with a completed NewGen Survey
  - o 1,605 Gulf-era Veterans with a completed NewGen Survey

- New Generation respondents who were also GW respondents. These are people who were sampled for and completed the baseline survey for both studies.
  - o 35 Gulf War Veterans who completed the 1995 survey also completed the baseline NewGen study