Presentation 8 – Lea Steele

Research on Treatments for Gulf War Veterans' Illnesses:

Background and Context

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GWI Treatment Research

- Challenges of studying GWI treatments
- Evaluating evidence re: treatment effects
- VA/DOD Clinical Practice Guidelines
- Treatment studies of GWI
- Identifying "new" treatments

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GWI Treatment Research

- Treatment Information we've discussed
  - ABT, EBT Clinical Trials
  - VA/DOD Clinical Practice Guidelines
  - Clinical experience at NJ WRIISC

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GWI Treatment Research

Evaluating GWI treatments is extremely challenging

- GWI may include multiple pathophysiological processes
  - May require treating concurrent problems that differ in different people
  - Which subgroups benefit from which treatments?
- No objective clinical markers of illness
- No accepted GWI case definition
  - Who has Gulf War illness/who does not?
- How best to measure health improvement/response to treatments?

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GWI Treatment Research

- Measuring Improvement: Outcome Measures
  - Change/elimination of biological indicator of pathology (e.g. infection)
  - Sustained symptom improvement
  - Improvements in functional status on standardized tests
    - SF-36, SIP, cognitive function, etc.
    - Exercise tolerance

GWI Treatment Research: Measuring Outcomes

- SF-36
  - Evaluates health/functional status in several domains of daily life
    - Physical function summary score (PCS)
    - Mental health function summary score (MCS)
  - Mean score in the general population is 50 (scale of 0-100)
  - Mean scores associated with diseases:
    - Diabetes = 42
    - COPD = 36
    - GWI participants in ABT trial = 30

Evaluating Evidence of Treatment Efficacy; Effectiveness

Levels of Evidence (IOM, 2001)

Level	
1	Multiple well-designed RCTs; multiple well-designed outcomes studies
2	Single well-designed RCT; single well-designed outcomes study
3	Consistent findings from multiple observational studies
4	Single cohort or case/control observational study
5	Unsystematic observation, expert opinion, consensus judgment

Gulf War Veterans' Illnesses: Treating Symptoms and Syndromes, IOM, 2001

GWI Treatment Research: Little Evidence to Evaluate

- VA/DOD Clinical Practice Guidelines: Recommendations of Expert Panels
  - Post Deployment Health Concerns
  - Medically Unexplained Fatigue and Pain
- VA/DOD Clinical Trials
  - EBT
  - ABT

VA/DOD Clinical Practice Guidelines: Medically Unexpl Fatigue and Pain

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF MEDICALLY UNEXPLAINED SYMPTOMS (MUS): CHRONIC PAIN AND FATIGUE

Guideline Summary

PRIMARY CARE

GUIDELINE SUMMARY

- Establish that the patient has MUS.
- Obtain a thorough medical history, physical examination, and medical record review.
- Minimize low yield diagnostic testing.
- Identify treatable cause (conditions) for the patient's symptoms.
- Determine if the patient can be classified as Chronic Multi-Symptom Illness (CMI) (i.e., has two or more symptoms clusters: pain, fatigue, cognitive dysfunction, or sleep disturbance).
- Negotiate treatment options and establish collaboration with the patient.
- Provide appropriate patient and family education.
- Maximize the use of non-pharmacologic therapies:
  - Graded aerobic exercise with close monitoring.
  - Cognitive behavioral therapy (CBT)
- Empower patients to take an active role in their recovery.

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Clinical Practice Guidelines: Medically Unexplained Fatigue and Pain

THERAPY INTERVENTIONS FOR FIBROMYALGIA

THERAPY INTERVENTIONS FOR CFS

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Clinical Practice Guidelines: Medically Unexplained Fatigue and Pain

PHARMACOLOGIC AGENTS FOR CFS/FM

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GWI Treatment Research: Clinical Trials

EBT: Exercise/Behavioral Therapy Trial

1,092 Gulf War veterans at 20 study sites; 12 mo. therapy

	SF-36 PCS improved 7 pts. or more	SF-36 PCS mean pts. improved
Usual care	11.5 %	-0.04
Exercise	11.7 %	0.97
CBT	18.5 %	0.59
CBT + exercise	18.4%	1.03

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GWI Treatment Research: Clinical Trials

ABT: Antibiotic Treatment Trial

491 Gulf War veterans at 26 study sites; 12 mo. doxycycline

	% improved 7 pts. on SF-36	mean SF-36 scores baseline, 12 mos	% mycoplasma neg. @ 18 mos
Doxycycline	18.0 %	30.2 → 32.0	90 %
Placebo	17.3 %	30.1 → 30.9	87 %

GWI Clinical Trials: No evidence of substantial improvement in veterans' health

- EBT:
  - CBT produced 7% more veterans with 7 pt. SF-36 increase, but less than 1 point mean increase
  - Exercise/CBT produced some symptomatic improvement
- ABT:
  - Similar % of treatment and placebo group had 7 pt. increase at 12 mos; mean SF-36 increase was ~ 2 points
  - Mycoplasma infection and GWI?

Identification of Treatments for GWI: Approaches Used by VA

Levels of Evidence (IOM, 2001)

Level
1 Multiple well-designed RCTs; multiple well-designed outcomes studies

2 Single well-designed RCT; single well-designed outcomes study

3 Consistent findings from multiple observational studies

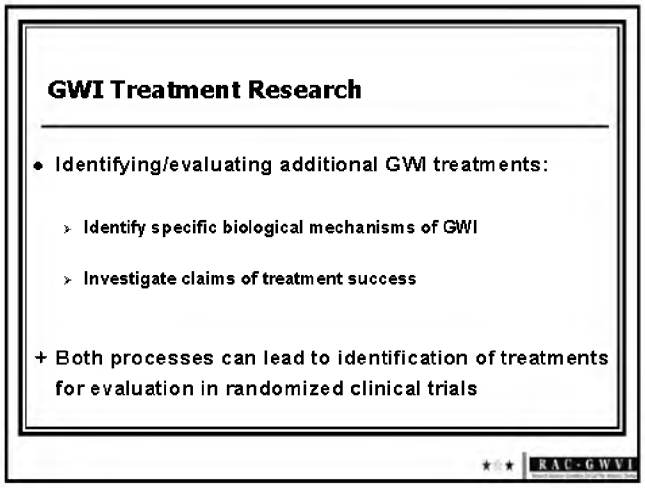
4 Single cohort/observational study

5 Unsystematic observation, expert opinion, consensus judgment

Gulf War Veterans' Illnesses: Treating Symptoms and Syndromes. IOM, 2001

GWI Treatment Research: What Next?

- Identifying/evaluating additional GWI treatments
  - **Identification of specific biological mechanisms underlying GWI**
    - Use existing treatments that counter those processes
    - Identify new pharmacologic interventions
  - **Systematic evaluation of treatments currently used; investigate claims of treatment success**
    - Gulf War illnesses
    - Similar multisymptom conditions


GWI Treatment Research
• Identifying/evaluating additional GWI treatments:
➢ Identify specific biological mechanisms of GWI
➢ Investigate claims of treatment success
+ Both processes can lead to identification of treatments for evaluation in randomized clinical trials
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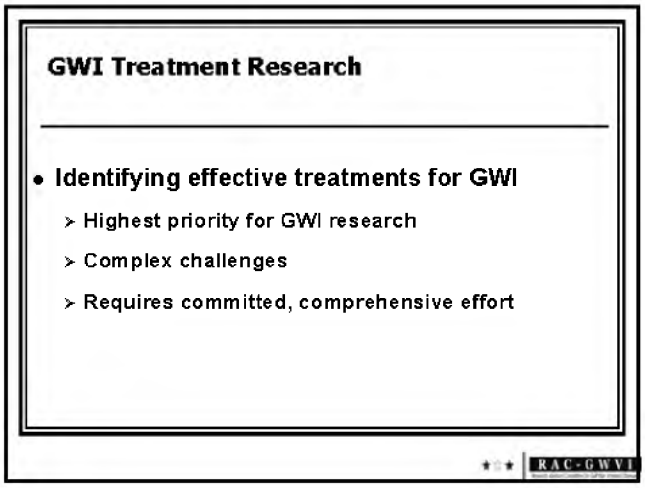
GWI Treatment Research
• Identifying effective treatments for GWI
➢ Highest priority for GWI research
➢ Complex challenges
➢ Requires committed, comprehensive effort
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