VA Cooperative Studies Program Contributions to National Healthcare

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Presenters

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Disclaimer

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Presentation Objectives

Describe the role of the Department of Veterans Affairs (VA) Cooperative Studies Program (CSP), and some of the Study Outcomes and their Impact on the VA and National Healthcare Systems.
In 1946, concerned with the health of 10,000 Veterans with Tuberculosis (TB), Drs. John Barnwell and Arthur M. Walker initiated a study to evaluate various drugs in the treatment of the disease, including the antibiotic Streptomycin.
Beginning of Cooperative Studies

- In 1955, the Perry Point VA Medical Center in Maryland developed a program for conducting cooperative studies in psychiatry.
  - The program emphasized the design and conduct of randomized trials for the treatment of chronic schizophrenia.
Beginning of Cooperative Studies

- In 1972 Cooperative Studies Program (CSP) was officially established to coordinate multicenter clinical trials that evaluated novel therapies or new uses of standard treatments.

- The first centers were established at Perry Point, MD and West Haven, CT.

- The clinical research pharmacy was also created; originally located in Washington, DC now in Albuquerque, NM.
Background

Through collaborative efforts within VA and with other federal, international, university, and private industry partners, CSP accomplishments have included key research findings across a range of diseases and have helped to provide definitive evidence for clinical practice within VA and the nation.
Background

- CSP serves as a Sponsor for conducting multi-disciplinary clinical trials that focus on addressing clinical problems and diseases prevalent in the Veteran population.
- Responsible for over six decades of major health advances.
Cooperative Studies Program

The VA Cooperative Studies Program (CSP) is now the division of VA Research and Development that is responsible for the planning and the conduct of large multi-center clinical trials and epidemiological studies within the Department of Veterans Affairs.
CSP Mission

To advance the health and care of Veterans through cooperative research studies that produce innovative and effective solutions to Veteran and national healthcare problems.
CSP Quality Policy

To improve Veteran and national healthcare by conducting cooperative research studies that are well-designed, produce high quality data, protect research participants and comply with applicable requirements and standards, while continuously improving the quality management system.
Quality - ISO Certification

- The ISO certification is an acknowledgement of exceptionally high standards in this area of quality management.
CSP Centers

Coordinating Centers
- Boston, MA
- Hines, IL
- Palo Alto, CA
- Perry Point, MD
- West Haven, CT

Epidemiological Centers
- Boston, MA
- Durham, NC
- Palo Alto, CA
- Seattle, WA
- West Haven, CT
Unique to CSP is the Clinical Research Pharmacy Coordinating Center, (CSPCRPCC) which provides additional resources for all CSP studies, specifically ones involving drugs or devices.
CSP Clinical Research Pharmacy Coordinating Center

- Liaison to the Food and Drug Administration, pharmaceutical and device industries.

- Responsible for Cooperative Research and Development Agreements (CRADAs), when required:
  - a CRADA is an agreement between a government agency and a private company or university to work together on research and development.

- Review, monitoring and medical coding of adverse and serious adverse events.
Network of Dedicated Enrollment Sites (NODES), 2012

A consortium of nine VA medical centers (Dallas, Hines, Houston, Long Beach, Minneapolis, Palo Alto, Portland, Salt Lake City and, San Diego) with dedicated teams that conduct studies to evaluate and enhance overall performance, compliance and management.
Network of Dedicated Enrollment Sites (NODES)

The NODES work together with the CSPCCs to share best practices and provide local insights on study design and related considerations that can help with study management and conduct.
CSP Model for Central Coordination

- Administrative and budgetary management
- Project management
- Study conduct
- Data collection and management
- Monitoring and compliance
- Quality assurance
Areas of Expertise

- Research Design
- Statistical Methodology & Analysis
- Data Management
- Computer Programming
- Biomedical Engineering
- Manuscript writing / Publications
VA’s Clinical Priorities

- Suicide Prevention
- Post Traumatic Stress Disorder
- Opioid / Pain Management
- Traumatic Brain Injury
Landmark Fields of Study

- Cardiovascular disease & surgery
- Endocrinology
- Gastroenterology
- Infectious diseases & surgery
- Mental health
- Oncology
Other CSP Center Studies

- Exoskeletons for VETS with Spinal Cord Injury.
- Support Dogs to Assist with Activities and Quality of Life in Veterans with PTSD
- Conducts Cooperative Clinical Trial Award (CCTA) Studies. Example...
- Cohort Studies
Examples of Significant Study Results

- Discovered the optimal strategy for prescribing the correct drug for hypertension.

- Long-term effects of coronary artery bypass surgery were defined in the most extensive study on record.

- Low dose aspirin can prolong the lives of patients who have had coronary artery disease.
Examples of Significant Study Results

- Angioplasty prevents chest pain in patients with mild heart disease and allows them to exercise more.

- Patients with heart failure can be saved with optimal drug therapy.

- Determined the optimal device for patients who require heart valve replacement surgery.
Examples of Significant Study Results

- Progression of HIV infection to full blown AIDS can be delayed with the drug AZT.

- Discovered which blood tests best determine if treatment for AIDS is effective.

- Patients with septic shock should not be given steroid therapy.

- Patients treated with chemotherapy and radiation rather than surgery for advanced throat cancer can keep their voice boxes.
Examples of Significant Study Results

- Discovered which medical treatment for enlarged prostate works best.

- An implanted insulin pump controls blood sugar better than multiple daily insulin injections.

- Discovered the most effective cochlear implant to help totally deaf patients hear and understand speech.
Examples of Significant Study Results

- Determined the best treatment for alcoholic patients with bleeding in the esophagus.
- Determined an effective alternative drug treatment for epilepsy.
- Surgery is an effective alternative to long term medical therapy for severe heartburn.
Examples of Significant Study Results

- Aspirin helps reduce heart attacks & death.
- Benign prostatic hyperplasia (prostate gland enlargement) can be relieved by Terazosin.
- Blood pressure can be managed with antihypertensive drugs in patients with cardiovascular disease.
Examples of Significant Study Results

- Clozapine is a cost-effective treatment for schizophrenia.
- Diabetics can have \( \uparrow \) quality of life using an insulin pump.
Examples of Significant Study Results

- CSP #589, Individual Placement and Support (IPS) services improve employment outcomes and occupational functioning for Veterans with posttraumatic stress disorder, as well as significantly improve functioning in the non-vocational areas of interpersonal relationships, daily lifestyle, and quality of life.
  - Implemented at the Louis Stokes Cleveland VA Medical Center as usual care.
Examples of Significant Study Results

- Nicotine Patch in partnership with UCLA, 1984
  - And more recently, nicotine patches are also under study to help relieve the symptoms of post-surgical pain, to treat early dementia, and to treat symptoms of ADHD.

- CSP #424 COURAGE Trial
  - Cardiac Study in Partnership with Canada. Percutaneous Coronary Intervention (PCI) (angioplasty with stent) + Optimal Medical Therapy (OMT) does not improve coronary artery disease outcomes compared to OMT alone.
Examples of Significant Study Results

- CSP #558, Robot-assisted therapy for stroke patients has the capacity for clinically relevant plasticity even in the chronic phase after a stroke.

- CSP #403, Shingles vaccine is effective in preventing shingles and reducing symptoms in patients with shingles.

- Warfarin helps prevent stroke.
Publications

- In the last 10 years,
  - there have been 105 primary papers from CSP studies
  - there have been 225 secondary and tertiary papers from CSP studies

- In the last 5 years,
  - there have been 190 staff publications on topics such as informed consent, and others not necessarily medically related but process related
Journals

- New England Journal of Medicine
- JAMA
- Lancet
- Internal Medicine
- American Journals of Epidemiology, Geriatric Psychiatry, Medicine, Gastroenterology
- Addition
- Sclerosis
- Infectious Disease
- Telemedicine, and more
- Internal Medicine
- Thoracic Surgery
- Dermatology
- Ophthalmology
- Clinical Trials
- Diabetes, and more
The Dynamics of a Study as it Pertains to West Haven CSP Coordinating Center (WH-CSPCC)
Dynamics

Study Team

Scientific Peer review

Organizational & Start-up

Execution
Enrollment -- Follow-up

Analyses & Close-out

Study Chair(s)
Biostatistician
Research Pharmacist
Health Economist

Project Manager
Research Associates
Programmers / DM

Site Investigators
Nurse/Site Coordinators
Executive Committee

IRB / R&D Committee
FDA
CSPCC HRC DMC

IRB / R&D

Scientific & Ethical review

Scientific & Ethical review

Scientific & Ethical review

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“Esketamine as a Next Step Treatment for Treatment Refractory Major Depressive Disorder in the VHA: Comparison with Aripiprazole”.
- Target: 25 sites / 940 Veteran participants.
- 3 months accrual / 3 months follow-up.
- Objective is to show adjunctive ketamine therapy vs. Aripiprazole will result in a significantly greater likelihood of symptom remission during an 8-week acute phase trial.
Planning

CSP #2018

“Growth Hormone Replacement Therapy in Veterans with mild Traumatic Brain Injury (mTBI) with Adult Growth Hormone Deficiency (AGHD)”.
Target: 20 sites / 177 Veteran participants.
27 months accrual / 6 months follow-up.
Goal is to study the efficacy and safety of rhGH replacement therapy as a treatment of patients with mTBI and AGHD.
Organizational & Start-up
Execution

Enrollment -- Follow-up
Active

CSP #2004

- Microbiota vs. Placebo after Antibiotic Treatment for C. difficile at Home (MATCH)

CSP #592

- Efficacy and Safety of ICD Implantation in the Elderly (I-70)
CSP #2004 MATCH Study

Microbiota or Placebo after Antimicrobial Therapy for Recurrent C. difficile at Home
CSP #2004 MATCH Aims

Primary Objective

- The primary study goal is to assess the efficacy of FMT for the prevention of subsequent recurrent CDI, when administered after successful treatment of recurrent CDI with standard antimicrobial therapy.
CSP #2004 MATCH
One Study Site Operating Nationally

Minneapolis, MN

West Haven, CT
CSP #2004 MATCH Study

Treatment Arms
- Fecal Microbiota Therapy (FMT)
- Placebo

Study duration
- 5 years (3 year accrual period, 6 month follow-up, 6 month closeout, 1 year analysis)

Target
- 390 Veterans (195 per treatment arm)
CSP #592, I-70 Study

Efficacy and Safety of ICD Implantation in the Elderly (I-70)
CSP #592, I-70

Primary Study Aims

- To determine if a primary prevention strategy with ICD implantation in addition to optimal medical therapy (OMT) is effective in reducing all-cause mortality compared to OMT alone in patients 70 years of age and older who are eligible for ICD therapy according to current Centers for Medicare & Medicaid Services (CMS) criteria.
CSP #592, I-70 Study

5 Study Sites, Plus 1 Central Follow-up Office

- Portland, OR and Central Follow-up Office
- Minneapolis, MN
- West Haven, CT
- Washington, DC
- Gainesville, FL
- Nashville, TN
CSP #592, I-70 Study

Treatment Arms

- Implantable Cardioverter Defibrillator
- Optimal Medical Therapy (OMT)

Study duration

- Ongoing Pilot Study – expansion to full study pending

Target

- 1462 (731 per treatment arm)
Follow-up

Colonoscopy vs. Fecal Immunochemical Test in Reducing Mortality from Colorectal Cancer

CONFIRM
CSP #577 CONFIRM

Primary Aim

To determine if a strategy of screening colonoscopy decreases Colorectal Cancer (CRC) mortality over 10 years in average risk adults as compared to annual fecal immunochemical test (FIT) screening.
Secondary Aims

- To determine if a screening colonoscopy decreases 10 year CRC incidence as compared to annual FIT screening
- To evaluate the safety of screening colonoscopy
Secondary Aims

- To evaluate the association between colonoscopists’ characteristics and the initial detection of colorectal neoplasia, complications and post-colonoscopy CRC.
CSP #577 CONFIRM Study

Treatment Arms

- Colonoscopy (one time screening)
- FIT (Annually)

Study Population

- Veterans ages 50-75
CSP #577 CONFIRM Study

Target

- 50,000 Veterans (25,000 per treatment arm)

Study duration

- 15 years, 5 year accrual period, minimum follow-up of 10 years
CSP #577 CONFIRM Study

The 50,000th Veteran was enrolled on November 15, 2017!

n=50,126 December 1, 2017
CONFIRM Sub-Study was approved 08/18/2016

Biorepository for future research opportunities
- Blood specimens
- Stool specimens
- Enrollment ended 09/30/2019

N=10,702 Blood Specimens Collected
CSP #577 CONFIRM Study

- Instrumental in helping the Veterans Health Administration's (VHA’s) initiative to increase CRC adherence to 80% by 2018.
- National Achievement Awardee, Jason Dominitz, MD (Study Co-Chair) – Colorectal Cancer Screening Champion.
New York City Jumbotron
Million Veteran Program

- MVP aims to be one of the largest programs on genes and health in the United States.
- Target n=1,000,000; over 5 to 7 years time period.
- MVP is a national, voluntary research program, designed to help researchers better understand how genes affect health and illness.
Researchers may use this information to learn how genes, lifestyle, and military experience affect health and disease.

Research findings based on MVP may lead to new ways of preventing and treating illnesses in Veterans and all Americans.
Analyses & Close-out
Analysis

- CSP #576 – “VA Augmentation and Switching Treatments for Improving Depression Outcomes” (VAST-D Study).

- CSP #589 – “Veterans Individual Placement and Support Towards Advancing Recovery” (VIP-STAR Study).
  - Strategy implemented

- CSP #572 - GWAS in Schizophrenia and Bipolar (assist CERC)

- CSP #565 - VA NEPHRON-D Study
THIS WE'LL DEFEND.
SEMPER FIDELIS.
UNO AB ALTO.
SEMPER FORTIS.
SEMPER PARATUS.
THANK YOU!

ARMY   MARINES   AIR FORCE   NAVY   COAST GUARD
Time to Play Jeopardy!
Jeopardy

Begins with “C”

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Results

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That Great State

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Sunny California

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Final Jeopardy
This type of trial generates data on safety and efficacy.

What is a “Clinical” trial.
This study with over 50,000 participants is titled this, which is a synonym for “verify”.

What is “CONFIRM”.
1 - $300

- The VA _____ Studies Program (CSP) is the Division of VA Research and Development responsible for the planning and the conduct of large multi-center clinical trials.

- What is “Cooperative”.
I - $400

- The CSP Coordinating Centers have received and maintain this from ISO.

- What is “certification”.
Boston, Hines, and Palo Alto are locations where the CSP maintains these _____ centers.

What are “coordinating”. 
This patch was found to be an effective method of smoking cessation.

What is a “nicotine” patch.
CSP proved the effectiveness of a vaccine developed for this viral infection caused by varicella-zoster.

What is “Shingles”?
This medication was found to help reduce heart attacks & death.

What is “Aspirin”.
Warfarin was found to prevent this.

What is “stroke”.
Using this type of pump was found to increase quality of life for diabetics.

What is an “insulin"
The presenters are from this great US state

What is: Connecticut
3 - $200

- He is the wealthiest living actor in Connecticut
- Who is: Seth MacFarlane
In 1844, the first use of this without sensation drug was made in Connecticut by Horace Wells.

What is: Anesthesia
3 - $400

- The birthplace of George W. Bush
- What is: New Haven, Connecticut
This world famous candy is made in the town of Orange, Connecticut

What is: PEZ
There is no view of the Bay like the one seen from the middle of this bridge

What is: The Golden Gate Bridge
From 1934 to 1938 Al Capone enjoyed the California weather & lifestyle at this location.

What is: Alcatraz
4 - $300

You can trace the history of the blue jeans at the Levi Strauss museum in this California city

What is: San Francisco
Carl Henry came up with the idea of using a curved street to help vehicles move downhill on this famous street.

What is: Lombard Street, in San Francisco
Get out of the city and feel the sea breeze on California Route 1 known for much of its length by this three-word oceanic name.

What is: Pacific Coast Highway
Final Jeopardy


- What is: the theme for SRAI 2019 Annual Meeting
Questions or Comments?
Resources

VA Cooperative Studies Program:
https://www.research.va.gov/programs/csp/default.cfm

ORD Timeline of Accomplishments:
https://www.research.va.gov/about/history.cfm

CSP A Legacy of Achievement:

Veterans Affairs Cooperative Studies Program - A report on
The Clinical Research Pharmacy Coordinating Center:
http://marketingreports.blogspot.com/2016/07/veterans-affairs-cooperative-studies.html