Bridging the Causeway: 
A Center for Healthcare Policy and Research Symposium

In cooperation with:
The Clinical and Translational Science Center
The Center for Reducing Health Disparities
and the Office of Research

University of California, Davis
Memorial Union
March 25, 2008
Center for Healthcare Policy and Research

Director: Klea D. Bertakis, M.D., M.P.H.

“The Mission of the CHPR is to facilitate research, promote education and inform policy about health and healthcare.

The Goals of this Mission are to improve the health of the public by contributing new knowledge about:

• access
• delivery
• cost
• outcomes”

“The CHPR is an interdisciplinary, collaborative research unit”
“Bridging the Causeway” workshop –

CTSC, CHPR and CRHP

- Lars Berglund, MD PhD
- Director, UC Davis CTSC
NIH and Institutions: Working together as a National Consortium

Advisory & Leadership
- IC Directors Advisory Board
- NCRR Director
- NCRR Advisory Council

Oversight
- Clinical
  - D. Asmuth
- Pediatrics
  - A. Philipps
- Consortium Oversight Committee
  - L. Berglund

Steering
- Informatics
  - K. Anderson
- Biostatistics
  - L. Beckett
- Clinical Research Ethics
  - A. Kon
- Translational
  - A. Tarantal
- Community Engagement
  - S. Aguilar-Gaxiola
- Evaluation
  - J. Rainwater
- Education/Career Development
  - F. Meyers
- Public Private Partnerships
  - K. Marusina

Advisory: providing guidance and input to the NCRR Director on the CTSA Consortium
Oversight: identifying and selecting collaborative opportunities to facilitate research throughout the CTSA program, coordinating Consortium-wide approaches to research and overseeing topic-specific efforts across the Consortium.
Consortium Opportunities:

- In depth knowledge of specific site strengths (faculty and core resources)
- Flexibility in leverage of resources within and across institutions
- Forum to share best practices and resources
- Mechanism to promote translational research education and projects
Consortium Activities

- Developing inter-CTSA collaborations through committee framework
- Providing national identity for translational science – common, unified voice
- Identifying mechanisms to make clinical trial/research environment more efficient
- Leveraging activity to facilitate NIH institute research programs
- Contribution to change in institutional culture
Transform research into medical discoveries

Eliminate silos and barriers

Integrate programs and activities

through a series of functions and programs

Research incubator

Research Education, Training and Career Development
Pilot and Collaborative Studies
Community Engagement
Regulatory Knowledge and Support
Biomedical Informatics
Participant and Clinical Interactions Resources
Novel Clinical and Translational Methodologies
Design, Biostatistics and Clinical Research Ethics
Translational Technologies and Resources

Transform research and improve health care

Medical discoveries

Basic Science Research
Animal Models/Pre-clinical Testing
Clinical Testing and Application
Community Outreach
Interdisciplinary projects
CTSC Evaluation and Tracking
Pilot grant program – 2008

- Pilot calls linked to workshops and symposia
- Inflammation workshop partnering with Cancer Center January 2008 – call for planning grants with new teams
- “Bridging the causeway”- workshop partnering with Center for Healthcare Policy and Research March 25, 2008 – calls focused on community research projects
- New technologies workshop – in development with CBST
• Engage faculty, students, fellows in translational research
• Provide opportunities through core facilities and resources
• Eliminate barriers by fostering collaborations

Transform research and improve health care

Eliminate silos and barriers

Integrate programs and activities

Translational Program

Research Incubator

Pilot and Collaborative Studies

Transform research and improve health care

Basic Science Research
Animal Models/Pre-clinical Testing
Clinical Testing and Application
Community Outreach

Research Education, Training and Career Development
Community Engagement
Regulatory Knowledge and Support
Biomedical Informatics
Design, Bioinformatics and Clinical Research Ethics
Participant and Clinical Interactions Resources
Translational Technologies, Resources, and Methodologies
CTSC Evaluation and Tracking

Interdisciplinary projects

Basic Science Research
Community Outreach
Clinical Testing and Application
Animal Models/Pre-clinical Testing

UC Davis Health System
Themes of community engagement and practice-based collaborative research

- Keynote: J. Westfall
- Health Services Research Sessions
  - Cancer
  - Obesity
  - Mental Health

Presented in Community Program
The Mission of the CRHD is to promote the health and well-being of diverse communities by pursuing:
- Research;
- Training;
- continuing education;
- technical assistance; and
- information dissemination
within a prevention, early intervention and treatment framework that recognizes the unique cultural and linguistic contexts of these populations.
The **Main Goal** is to create and foster an innovative research environment in which:

- new, scientific and practical understandings of health disparities can be achieved;
- the knowledge generated can be translated, shared (through education and training) and disseminated; and
- new approaches to reducing these disparities can be developed for implementation throughout California and beyond.
Thematic Overview:

• Obesity
• Cancer
• Mental Health
Obesity: basic questions about diets have not been answered.

Craig Warden, Ph.D.
Professor of Pediatrics, Physiology and Genetics
Benefits and Risks of Popular Weight Loss Diets

The A TO Z Weight Loss Study

(Community Foundation SE Michigan)

Christopher Gardner, PhD

Stanford Prevention Research Center
Stanford University, Department of Medicine
12-month net weight change (kg): Individual
Weight loss is feasible on a wide range of diets, from very-low, to intermediate, to very-high carbohydrate.
Favored Atkins
(Weight)
HDL-C
SBP
DBP

Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults
Obes Res 1998;6(Suppl)2:51S-209S.
Individual differences between total fat loss on a very low-carbohydrate ketogenic (VLCK) diet minus total fat loss on a low-fat (LF) diet for each person. Positive numbers reflect greater weight loss on the VLCK, whereas negative numbers indicate greater weight loss on the LF diet. Red circles = order of diets VLCK then LF. Blue diamonds = order of diets LF then VLCK. Volek et al. Nutrition & Metabolism 2004, 1:1-13.
Conclusions Over a mean of 8.1 years, a dietary intervention that reduced total fat intake and increased intakes of vegetables, fruits, and grains did not significantly reduce the risk of CHD, stroke, or CVD in postmenopausal women and achieved only modest effects on CVD risk factors, suggesting that more focused diet and lifestyle interventions may be needed to improve risk factors and reduce CVD risk.

Bethesda, we have a problem.
You are what you eat...

Eat fat, get fat

Dietary Fatty Acid Composition → Circulating/Tissue Fatty Acid Composition

More potential for harm
Blood Saturated Fat Levels

Low Fat Diet
- 12 g SFA/d
- 208 CHO/d

High Fat Diet
- 36 g SFA/d
- 45 CHO/d
Blood Saturated Fat Levels

- Low Fat Diet (208 g CHO/d)
  - Saturated Fat Synthesis
  - Saturated Fat Intake (12 g/d)

- Low Carbohydrate Diet (45 g CHO/d)
  - Saturated Fat Synthesis
  - Saturated Fat Intake (36 g/d)

Saturated Fat Burned as Fuel
Despite a >3-fold greater intake of saturated fat...

...a low carbohydrate diet results in a 2-fold greater reduction in total saturates in triglycerides.

It’s what you do with the fat that matters!

Clinton R Bruce & Mark A Febbraro

Obesity and a diet rich in saturated fatty acids can lead to high lipid levels in the liver and insulin resistance. However, inhibition of a key enzyme that elongates long-chain saturated fatty acids can protect against insulin resistance in fatty livers, even with concurrent obesity (pages 1193–1202).

*NATURE MEDICINE* VOLUME 13 | NUMBER 10 | OCTOBER 2007
You are what you do with what you eat!

Eat fat, lose fat

Dietary Fatty Acid Composition \rightarrow\text{Circulating/Tissue Fatty Acid Composition}

Endogenous processing, controlled to a large extent by CHO
Reasons to use animal models

• Because some important studies would be unethical in humans.

• For example:

• Environment: Rigorous control for large Ns.

• Mechanism: (1) Collect any tissues at any time; (2) Quickly determine effects of diverse diets or exercise on metabolism; (3) Intentional genetic modifications – transgenics and knockouts.

• Maternal effects: (1) Large N adoption studies of nurse-mother genetic and environmental effects; (2) Feeding high fat diets to pregnant mothers.
Effects of varying ratios of fat and carbohydrate on obesity and liver health in C57BL/6J mice.

- 5 treatment groups of 8 C57BL/6J mice each were fed one of five diets ad libitum for 4 weeks.
- Food cups were changed daily, daily food intake data was collected, and body weights were taken on a weekly basis.
Relative Liver Weight and Adiposity Index of B6 Mice Fed Percentages of Dietary Fat

AI = total fat weight/body weight.  LWT = liver weight. BWT = body weight.

Percent Dietary Fat (%Kc)

Ave LWT/BW
Ave AI100
Specific recommendations

• Humans: Genotype will influence obesity and response to diet. Thus, collect consented DNA from large N human trials.

• Conduct randomized trials to test a wide range of diets and exercise.

• For animal models: Develop diets that better model human food.

• Specific research questions:
  • Diets – Systematic studies are needed to determine how composition (type and amount) of diet influences weight and other phenotypes!
  • Maternal effects. Which has a larger population impact – maternal environment or maternal genetics?
Thematic Overview:

• Obesity
• Cancer
• Mental Health
CANCER PREVENTION RESEARCH

Bench to Bedside -- Not Enough?
Joy Melnikow, MD, MPH

Center for Healthcare Policy and Research
Department of Family and Community Medicine
University of California, Davis

Funded By:
National Cancer Institute, California Breast Cancer Research Program, UC Davis CTSC
Collaborators

• Tamoxifen
  Christina Slee, Jay Helms, Miriam Kuppermann, Stephen Birch, James Nuovo, Amber Barnato

• HPV vaccine
  Teresa Farley, Debora Paterniti
Barriers to Implementation

• Weighing benefits, harms and costs
  – Tamoxifen for breast cancer risk reduction

• Preferences, information, and decision making
  – HPV vaccine
Tamoxifen
Tamoxifen

• Synthetic estrogen receptor modulator (SERM)
  – Used for adjuvant treatment of hormone sensitive breast cancer

• Breast cancer risk reduction
  – RCT with 13,338 women over 5+ years
  – 50% reduction in incidence of breast cancer

• 1998: FDA approved for breast cancer risk reduction for women with 5-year risk >1.67%
Tamoxifen Outcomes

Potential Benefits
- ↓Breast cancer
- ↓Osteoporotic fractures
  (↓Long-term disability from hip fracture)

Potential Harms
- ↑Endometrial cancer
- ↑PE
- ↑DVT
- ↑Cataracts
- ↑Menopausal symptoms
Research Question

• What are the projected benefits and harms over time from tamoxifen in women with population baseline risks?
• What is the cost-effectiveness of tamoxifen:
  – for women with population baseline risks?
  – When effects on quality of life are considered?
Methods

- Markov cost-effectiveness model
  - Used population-based risk estimates
  - Monte Carlo analysis projected outcomes at 10 and 50 years
  - Considered direct healthcare costs
  - Incorporated quality-of-life effects
### Monte Carlo Analysis

**Projected outcomes**

<table>
<thead>
<tr>
<th>Clinical Events</th>
<th>10-year Time Horizon</th>
<th>Lifetime Time Horizon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>No Tamoxifen</td>
</tr>
<tr>
<td>Invasive breast cancer</td>
<td>83</td>
<td>160</td>
</tr>
<tr>
<td>DCIS</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>124</td>
<td>43</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>Pulmonary embolism (PE)</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>Deep venous thrombosis (DVT)</td>
<td>39</td>
<td>29</td>
</tr>
<tr>
<td>Cataracts</td>
<td>117</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>No Tamoxifen</td>
</tr>
<tr>
<td>Invasive breast cancer</td>
<td>417</td>
<td>500</td>
</tr>
<tr>
<td>DCIS</td>
<td>85</td>
<td>102</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>270</td>
<td>189</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>846</td>
<td>851</td>
</tr>
<tr>
<td>Pulmonary embolism (PE)</td>
<td>140</td>
<td>121</td>
</tr>
<tr>
<td>Deep venous thrombosis (DVT)</td>
<td>251</td>
<td>241</td>
</tr>
<tr>
<td>Cataracts</td>
<td>1122</td>
<td>1091</td>
</tr>
</tbody>
</table>
## Monte Carlo Analysis
Projected Mortality

<table>
<thead>
<tr>
<th>Clinical Events</th>
<th>10-year Time Horizon</th>
<th>Lifetime Time Horizon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>No Tamoxifen</td>
</tr>
<tr>
<td>Breast cancer death</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Uterine cancer death</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Hip fracture death</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>PE death</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

|                 | Tamoxifen            | No Tamoxifen          |
| lifetime Horizon | 67                   | 82                    |
| lifetime Horizon | 33                   | 22                    |
| lifetime Horizon | 135                  | 136                   |
| lifetime Horizon | 28                   | 24                    |
Projected 10 year mortality for tamoxifen-related outcomes and all other causes for women with 5-year breast cancer risks of 1.67%, 3% and 5%
ICER by 5-Year Breast Cancer Risk Using Outcome-specific Utilities

- No treatment side effects w/uterus
- No treatment side effects w/o uterus
- Menopausal symptoms w/uterus
- Menopausal symptoms w/o uterus

5-Year Breast Cancer Risk (%)

ICER ($/QALY)
Conclusions

• Overall difference in outcomes very small except for women at very high risk of breast cancer

• Drug pricing has a large impact when medications are taken for prevention

• Consideration of side effects affecting quality of life markedly reduces projected cost-effectiveness
Human Papillomavirus

- Non-enveloped, encapsulated double stranded DNA virus
- Infects human epithelial cells
- Over 100 viral types
- Specific types strongly related to cervical cancer. “High risk types”:
  - 16, 18, 31, 33, 35, 39, 51, 52, 59, 68, etc.
  - Type 16 and 18 cause 70-80% of cervical cancers in the US
Merck HPV Vaccine

Future II: Combined 4 RCTS:
20,583 women

Efficacy against 16/18 related disease:
• Intent to treat 44% (31 to 55%)
• Susceptible 98% (93 to 100%)
• Per protocol 99% (93 to 100%)

Merck HPV Vaccine

Future II:

Overall efficacy against CIN 2/3 or AIS: 18% (7-29%)

HPV Vaccine

- FDA approval 2006
- Aggressive marketing by Merck
- Controversy about school entry requirements
HPV Vaccine Study

Research Question:

• What are the information needs and preferences about the HPV vaccine for low income parents of middle school girls?
HPV Vaccine Pilot Study

Qualitative Methods:

- 8 focus groups – 4 completed
- African American, Caucasian, Hmong and Latina Sacramento parents of middle school daughters
HPV Vaccine Pilot Study

“When I took my daughter for her check up, the doctor talked to me about it, asked if she should do it, she gave me some information, and well based on what she told me, I told her to go ahead, and they gave it to her right there.”

*Latina mother*
HPV Vaccine Pilot Study

“I think for me it’s – I feel that this has such moral implications for me that, and my daughter to get it at 11and12, for me to talk about, you know, how it’s linked to sexual activities, it’s going to be difficult for me to sort of lead her down that path”

-Hmong mother
HPV Vaccine Pilot Study

“….if they know you have this allergic reaction to yeast, well, then once again, we don’t know the ingredients so it, it has something to do with yeast apparently and so they know some things, but it’s like they’re not letting all the information out because at the same time they don’t want to scare us. But we’re already scared because there’s too many unanswered questions.”

-African American mother
HPV Vaccine Pilot Study

Conclusions to date:

• Parents are hungry for information
  – both potential benefits and potential harms and side effects
• Physicians are a highly trusted information source
• Perception that vaccinating your daughter involves discussing sex is a barrier for some parents
Barriers to Implementation

• Baseline risks in general population differ from RCT’s
• Benefits and harms may weigh differently in the real world
• Costs
• Lack of information
• Patient preferences
Implementation Research
Finding the Way

• Define real world benefits and harms
• Consider costs and cost effectiveness
• Develop effective strategies for educating and empowering providers and patients
• Understand and respect patient preferences
• Consider alternate routes
Thematic Overview:

• Obesity
• Cancer
• Mental Health
Examining Cultural Factors within the Context of Evidence-Based Practices

Nolan Zane, Ph.D.
University of California, Davis
Department of Psychology
Asian American Center on Disparities Research
Mental Health Disparities

The 1978 president’s commission on mental health to the surgeon general (2001) and the president’s new freedom commission (2003) reports examined ethnic disparities in mental health. The reports concluded that the disparities were not so much due to racial and ethnic differences in rates of psychopathology but were due to inaccessible and ineffective treatment.
A recent study reviewed 379 NIMH-funded clinical trials published between 1995 and 2004 in five leading mental health journals (Mak, Law, Alvidrez, & Perez-Stable, 2005). The investigators found that less than half of the studies provided information on the specific ethnic composition of their samples.

Among those that specified their ethnic composition, most ethnic minority groups were underrepresented, notably Asian Americans, Hispanics, and Native Americans. White Americans continued to dominate as participants in clinical trials (61% in studies that provided specific ethnic information), and few studies analyzed for ethnic and cultural effects.
Specific Factors Approach to Cultural Competence

- Culture maps onto specific social psychological factors that influence treatment (Betancourt & Lopez, 1993)

- Certain factors related to the cultural experiences of ethnic minority clients affect specific aspects of treatment (e.g., credibility, self-disclosure)

- Applying and accounting for such factors adds to our clinical conceptual tools, enhances cultural competence, and “individualizes” treatment
Examination of Cultural Influences in Mental Health Service and Treatment

Aspect of Culture: Value Orientation

Domain of Functioning: Client-Therapist Relations

Cultural Issue: Shame & Face Issues

Critical Treatment/Service Issues: Client Engagement, Family Engagement, Treatment Adherence
Face

- Face -- face has been identified as a key and often-dominant interpersonal orientation in Asian social relations. As social beings, people are invested in presenting to others, either implicitly or explicitly, certain claims about their character in terms of traits, attitudes, and values. Others come to recognize and accept the person’s “face” or “line” that the person claims for her or himself. This set of claims constitutes that person’s face.
### Face Concerns and Self-Disclosure in Treatment

#### Beta Weights of Predictors for Different Types of Self-Disclosure

<table>
<thead>
<tr>
<th>Outcome Predictors</th>
<th>Personality</th>
<th>Neg. Self</th>
<th>Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Counselor Age</strong></td>
<td>.08</td>
<td>.04</td>
<td>.09</td>
</tr>
<tr>
<td><strong>Counselor SES</strong></td>
<td>.00</td>
<td>-.01</td>
<td>-.03</td>
</tr>
<tr>
<td><strong>Understandable</strong></td>
<td>.11</td>
<td>.14</td>
<td>.12</td>
</tr>
<tr>
<td><strong>Speech Clarity</strong></td>
<td>.07</td>
<td>.05</td>
<td>.04</td>
</tr>
<tr>
<td><strong>Diff. Following</strong></td>
<td>.05</td>
<td>-.01</td>
<td>.00</td>
</tr>
<tr>
<td><strong>Ethnic Match</strong></td>
<td>.25*</td>
<td>.26*</td>
<td>.17</td>
</tr>
<tr>
<td><strong>Gender Match</strong></td>
<td>.07</td>
<td>.09</td>
<td>.20*</td>
</tr>
<tr>
<td><strong>Loss of Face</strong></td>
<td>-.21*</td>
<td>-.22*</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>.31**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adjusted R²</strong></td>
<td>.03</td>
<td>.10</td>
<td>.11*</td>
</tr>
</tbody>
</table>

**Note:** N = 128

*p < .05, **p < .01, ***p < .001
FACE WORK
Avoidance of Threats to Face

- Direct avoidance of certain relationships
- Use of intermediaries
- Careful monitoring of conversation
- Self-restraint in expression
- Modesty and self-effacing to reduce likelihood of being discredited
FACE WORK
Avoidance of Threats to Face

- Use of respect, politeness, and courtesies as protective maneuvers
- Explanations and warnings to depersonalize face-threatening incident
- Denial or not recognizing that face-threatening event has occurred (tactful overlooking)
- Hiding or concealment of activity when person has lost control of expressions
Cultural Variations in Emotion Regulation

- Suppression was used less frequently in daily life by women holding Western European values as compared to women with bicultural Asian-European values (Butler et al., 2007)

- Suppression was associated with fewer self-protective goals and lower levels of negative emotion for the women with bicultural Asian-European values

-Suppressors with more bicultural values were seen as less hostile and withdrawn and more responsive than suppressors with European values
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University of California, Davis
Memorial Union
March 25, 2008
CHPR - CTSC PILOT GRANTS

• Supported by OVCR and CTSC
• Funds up to $10,000 per grant
• Up to 7 awards
CHPR - CTSC PILOT GRANTS

• Important problems in human health

• Implementation and dissemination
  – Community and public health levels

• Interdisciplinary collaboration

• Preliminary data for extramural proposals
CHPR - CTSC PILOT GRANTS

• Sponsored by OVCR and CTSC
• Funds up to $10,000 per grant
• Up to 7 awards
• Due date: May 19, 2008
CHPR - CTSC PILOT GRANTS

• Who are eligible PI’s?
  – Academic Senate and Adjunct Faculty
• Encouraged
  – Junior faculty
  – Established faculty moving into new areas
  – Collaboration with community or public health organizations
CHPR and CTSC PILOT GRANTS

- Applications:
  - In your packet
  - Online:

  - www.ucdmc.ucdavis.edu/chpr/events/pilot_grant_application.doc
Breakout Groups

Cancer – Garrison Room

Mental Health – Fielder Room

Obesity – DeCarli Room