Guidelines for Student Doctoral Research Projects in area of <u>Prevention-Only Treatable Disease (P-O.T.D.)</u> Doctoral of Physical Therapy Program, UML

Research Methods Course: 34.616 - Spring 2012 Professors Robert Karasek and Sean Collins

The Suggested Approach for Student Research Projects in the area of:

"Prevention-Only Treatable Disease (P-O.T.D.): 'High-level' causation of chronic disease and suitable high-level prevention and intervention strategies."

The main point of the P-O.T. D. approach is to lift the priority of primary prevention through development of a more elaborate explanation of how the physiological processes operate which are close to (i.e., proximal to) social causes of chronic disease operate. This will allow cases of risk to be more directly treated by limiting these social risks.

A. Chronic disease topic areas:

- 1. Asthma
- 2. High Blood Pressure
- 3. Fibromyalgia
- 4. Chronic Fatigue Syndrome
- 5. Observed drug side effect problems with major chronic disease drug treatments
- B. Typical social settings causing stress: work/ family/ social conflict or exclusion

Steps in Project Definition and research material analysis

1. Step I: Understand general principles of social stress exposure and physiological response Specific focus: stress effects on autonomic regulation (a "high-level" cause).

Sources are available on the project wiki page: <u>http://sean-collins.wiki.uml.edu/POTD</u>

<u>2. Step II: Review risk factors and models of the disease process</u> for one (or two) of the disease categories above: asthma, high blood pressure, fibromyalgia, and chronic fatigue syndrome. You will need to understand: (a) detailed mechanism for the disease process, (b) manifestations of the disease, and (c) risk factors for the disease - all at multiple levels of the disease.

You will need to understand the different model Mechanisms on the basis of relative High or Low level physiological status: i.e. biochemical (- low level), autonomic parasympathetic deficits (- high-level). The Table below rather arbitrarily locates seven levels of physiological functioning - to help students to orient to the concepts of High and Low-level explanations (we are only using this as a logical explanatory aide - not as a proven scientific classification system in this instance).

For example: high level manifestations of chronic disease could include fatigue, exhaustion, burnout, diffuse and undefined pain, panic/anxiety attacks, depression, ventricular fibrillation, asthma attacks. Lower level manifestations of chronic disease could include tissue damage associated with clear physical exposures, calcium channel deficiencies related to cardiac output pacing.

3. Step III. Review the literature and determine the "level-of explanation" presented You will review case studies, study research reports and published findings (and possibly, later in the process: interview health practitioners, organizational consultants in the area selected). 1. How much evidence does the research source give that "lower-level" mechanism of deficiencies can be clearly identified as the sole cause of the disease - without many "unresolved details."

There can be very much literature of this type, but for this project, students can rather quickly skim past these materials (we understand that voluminous evidence often does already exist).

However, the "unresolved details" can be very important: it is here that even major wellknown research can have failed to observe the processes we are looking for.

2 .What evidence is presented which is inconsistent with low-level explanations/mechanisms.3. What evidence exists for high-level mechanisms as cause of the disease.

<u>This is primarily what we a looking for</u>. However to really fit the P-O. T. D. approach, there should also be a stress exposure or subject exhaustion state involved.

<u>4. Step IV. Review of stress context/ subject exhaustion status</u> from the literature: either as clearly presented, or as indirectly inferred.

1. Since the stress explanations are relatively new, particularly related to work stress in the US literature, often there may be relatively little explicit direct material about the actual stress state for the subjects. Thus, of course is a very serious problem for this focus for a research paper: much, otherwise interesting literature will simply have to be overlooked because there is no information at all, and no way to indirectly infer a 'stress context' from very limited information that may be included with the article.

You may have to become a bit of a "detective." Often there is some material on the stress context - and thus the article or case can still be potentially "salvaged."

2. Equally important, and possibly somewhat easier to infer in much literature, is the "exhaustion status of the subject." This is also a relevant contributor to the P-O. T. D. process.

5. Step V. Search for Multi-level disease process linkages and examples of Controller/Controlled physiological relationships

One of the important issues for P-O.T.D. is that physiological systems exhaust their ability to precisely control (self-regulate) their Target physiological processes - after "exhaustion" of their ordering capacity. This capacity must then be restored in cycles of relaxation; i.e. cycles of activity and relaxation.

This implies multi-level relationships between physiological systems. These multi-level processes may be evident in some of the research literature you examine. If so, this would be very important to understand and document.

One example is the fact that the variability of the cardiac output (HRV) allows the blood pressure to be adjusted so that the pressure is optimal for the changing environmental demands of the subjects (for example: increasing HR when a person rises from supine to upright position). In the attached Figure 2 we show a number of Controller/Controlled relationships (4 stages) - as an example of some of the stages in the disease process (and by implication prevention/improvement processes) that you might find, at least in fragments, in your literature.

<u>6. Step VI. Prevention-related Processes as Interventions (so called "Complementary and Alternative Medicine" CAM by NIH):</u>

To restate from above: the main point of the P-O. T. D. approach is to lift the priority of primary prevention, though development of more elaborated explanation of how the physiological processes close to (proximal to) social causes of chronic disease operate - so that cases of risk can be directly treated by limiting the social risks.

Thus we need to insure that the logical review of the literature includes the following steps: A. Discussion of the relationship to the subject(s)' personal or social stress context:

1. Social situation stressor exposure and difficulty

(Refer to the general stress research literature to understand the breadth of this).

B. Discussion of the relationship to exhaustion

1. Evidence for exhaustion state of subject (s)

2. Understanding of the general techniques for restoring "control capacity (i. e., resting/restoration): information about rest breaks, vacations.

VII. Source Materials:

Archive Package given to class students on February 21, 2012 (see Appendix):

(a) Directly relevant papers (SC and RK)

(b) Recent PPT lectures in PT dept (RK)

(c) Past PPT lectures (SC and RK)

(d) Examples of case studies reviewed by students

(e) - TBA

III. Status of the Evidence: 2nd Law Control Capacity Limit Evidence Through Seven Levels of a Human Physiological Function

LEVEL	STATUS OF EVIDENCE	EXAMPLE
Level 1 Simple Organic Molecule Creation	2nd Law Limit Evidence	[Photosynthesis]
Level 2 Complex Protein Creation	2nd Law Limit Evidence	Amino acids into <u>complex proteins and</u> enzymes
Level 3 Environmentally Modulated Protein Synthesis Systems	?- 2nd Law Tests could be designed	Calcium channel linkages between heart muscle cells(?).
Level 4 Organelles and Single-cell Organisms	? - (plasmodial slime mold)	(1) Single-cell organisms. (2) <u>multi-cell</u> differentiations: "stomach cavity"
Level 5 Centrally-controlled Molecular-level Physiological Processes within Complex Organisms	?- 2nd Law Tests could be designed	<u>Centrally-controlled metabolism via</u> Insulin-based circulatory system.
Level 6 Environmentally Modulated Macro-Control of Organ Systems	2nd Law Limit Consistent Evidence	Autonomic regulation of cardiac output.
Level 7 Organism's Maintenance of Internal Stability in Environmental Adaptation	2nd Law Limit Consistent Evidence	Chronic disease and low workplace and social control evidence - (next section)



