

## **Section: Contact Information**

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## **Section: Project Requirements and Description**

### ***Group: Requirements to submit AOI***

A comprehensive review of previously published data has been completed. : **Yes**

The specific aims are clear and focused. : **Yes**

The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator. : **Yes**

The investigator agrees to develop an initial draft of the concept proposal within 6 weeks of approval of the AOI and to finalize the concept proposal within 6 months. : **Yes**

Project Title : **Clinical utilities of various prediction performance measures -- a case study of the CHF risk scoring system.**

Planned research population (eligibility criteria) :

**CCSS original cohort**

Proposed specific aims :

**Clinical decisions on disease management and early intervention are increasing guided by risk scoring systems, which entail an urgent need for a better understanding and utilization of various performance measures for risk prediction models by both clinicians and statisticians. The CCSS study by Chow et al. (2015, JCO) developed nine risk scoring systems for predicting future CHF events in childhood cancer survivors, where time varying area under the receiver operating characteristic curve (AUC, by Heagerty et al. 2000, Biometrics) was used as the model performance measure. We propose to assess these risk scoring systems as well as guide the selection of risk scoring systems with alternative performance measures, including the newly proposed average positive predictive values (AP, by Yuan et al., 2015, Front Public Health), the integrated discrimination improvement (IDI, by Pencina, 2008, Stat Med), and the net reclassification improvement (NRI, by Cook et al. 2009, Ann Intern Med). Each performance measure prioritizes different aspects of model performance. AUC focuses on the two probability density functions of risk scores in cases and**

controls, which does not directly measure prediction performance (or the lack of it) for individual patient. It is known that AUC may not be sensitive enough to differentiate risk scoring systems (Uno et al. 2013 Stat Med). An alternative measure AP summarizes the positive predictive value, which has direct clinical utility, of risk scores over their entire range. Thus, it emphasizes the scoring system's overall predictive ability for individual patient, which is appealing to clinicians. When our goal is to assess how much predictive ability is gained by including additional clinical information and/or whether to recommend a more complicated scoring system over a simpler scoring system in clinical practices, e.g. heart dose model vs. standard model, standard/heart dose model vs. simple model in Chow et al ., integrated discrimination improvement (IDI), and net reclassification improvement (NRI) could be very helpful.

In this study, we propose to 1) illustrate the four different performance measures for the nine risk scoring systems; 2) compare and discuss the clinical utilities of these alternative measures using these nine risk scoring systems as examples; 3) make informed recommendations based on clinical needs. This work has important implications for the evaluation of current and future risk models that will be developed from the CCSS for other health outcomes.

Will the project require non-CCSS funding to complete? : **No**

If yes, what would be the anticipated source(s) and timeline(s) for securing funding? :

**Group: Does this project require contact of CCSS study subjects for:**

Additional self-reported information : **No**

Biological samples : **No**

Medical record data : **No**

If yes to any of the above, please briefly describe. :

**Group: What CCSS Working Group(s) would likely be involved? (Check all that apply)**

Second Malignancy :

Chronic Disease :

Psychology / Neuropsychology :

Genetics :

Cancer Control :

Epidemiology / Biostatistics : **primary**

### **Section: Outcomes or Correlative Factors**

Late mortality :

Second Malignancy :

**Group: Health Behaviors**

Tobacco :

Alcohol :

Physical activity :

Medical screening :

Other :

If other, please specify :

**Group: Psychosocial**

Insurance :

Marriage :

Education :

Employment :

Other :

If other, please specify :

**Group: Medical Conditions**

Hearing/Vision/Speech :

Hormonal systems :

Heart and vascular : **Primary**

Respiratory :

Digestive :

Surgical procedures :

Brain and nervous system :

Other :

If other, please specify :

**Group: Medications**

Describe medications :

**Group: Psychologic/Quality of Life**

BSI-18 :

SF-36 :

CCSS-NCQ :

PTS :

PTG :

Other :

If other, please specify :

**Group: Other**

Pregnancy and offspring :

Family history :

Chronic conditions (CTCAE v3) :

Health status :

**Group: Demographic**

Age :

Race :

Sex :

Other :

If other, please specify :

***Group: Cancer treatment***

Chemotherapy :

Radiation therapy :

Surgery :

**Section: Anticipated Sources of Statistical Support**

CCSS Statistical Center :

Local institutional statistician : **Yes**

If local, please provide the name(s) and contact information of the statistician(s) to be involved. :

**Dr. Yutaka Yasui**

**Yan Chen**

Will this project utilize CCSS biologic samples? : **No**

If yes, which of the following? :

If other, please explain :

**Section: Other General Comments**

Other General Comments :