NCI Division of Cancer Control and Population Sciences
2011 New Grantee Workshop Poster Abstracts

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Bayesian Integrative Methods for High-dimensional Genomics Data

Jeffrey Morris, PhD; Keith Baggerly, PhD; Kevin Coombes, PhD

Due to recent technological advances, which are continuously decreasing in cost, various types of genomic, epigenomic, transcriptomic and proteomic data with different sizes, formats, and structures have become available. Among these are SNP arrays, gene expression microarrays, tiling arrays, noncoding RNA arrays, methylation arrays, and next generation sequencing. Each of these distinct data types provides a different, partly independent and complementary, high-resolution view of the whole genome. However, understanding the complex functions of the genes, proteins and other aspects of the genome requires more information than provided by the individual assays. Integrating data from different sources is, therefore, an important part of current research in biostatistics and bioinformatics research. In addition, data integration also plays an important role in combining clinical, environmental, and demographic data with informatics data, in order to improve medical decision making. A key task to this end, is to develop flexible and efficient quantitative models utilizing the underlying dependence structure of these high-throughput assays. We develop innovative statistical models not only to model assay-specific information but also to combine the information across assays and clinical information – thereby facilitating better understanding of the underlying biological mechanisms and hence improve cancer patient care.

Breast Cancer Prevention through Weight Control among Rural Breast Cancer Survivors

Jennifer Klemp, PhD; Carol Fabian, MD; Debra Sullivan, PhD; Kathryn Schmitz, PhD; Michael G. Perri, PhD; Theresa Shireman, PhD

Women who are obese at breast cancer diagnosis have a 1.5 to 2.5 increased risk of recurrence and death compared to their normal weight counterparts. Moreover, weight gain and decreased physical activity are common after diagnosis and also increase the likelihood of breast cancer recurrence and death. Rural women suffer from health disparities in breast cancer diagnosis and treatment. Women of the most rural counties also have the highest prevalence of obesity compared to urban women. To address these disparities, the overarching objective of this proposal is to develop a clinically effective and cost efficient strategy for delivering a weight control intervention to rural breast cancer survivors. Group phone-based treatment via conference call is a novel treatment delivery approach that we have shown to be effective for initial weight loss among rural breast cancer survivors and more effective than the standard individual phone-based approach among rural women. This innovative method of providing group treatment addresses access barriers in rural areas and may be especially ideal for rural breast cancer survivors because it provides social support in conjunction with a level of anonymity. Rural breast cancer survivors are more likely to be isolated, to have heightened concerns about privacy, and to report difficulty adjusting to breast cancer. At the same time, they have less access to professional support services, and thus are more likely to have unmet support needs surrounding both cancer and weight management. The opportunity to engage in lifestyle change with other survivors by phone may provide social support in a confidential setting at the same time it enhances diet, physical activity, and weight, as well as quality of life. However, the impact of group phone counseling during extended care for weight loss maintenance beyond 6 months remains unknown. Weight loss maintenance is the more challenging phase of treatment when weight regain is common, and this regain presents a potential risk for breast cancer recurrence. This randomized controlled trial will evaluate the effects of group phone-based treatment for weight loss maintenance among rural breast cancer survivors, compared to an established mail-based education comparison condition, subsequent to a 6 month group phone-based weight loss phase for both conditions. In addition to the intervention impact on weight loss maintenance, the study will provide estimates of incremental cost-effectiveness per kg loss between the two conditions and the impact on secondary outcomes including quality of life, breast cancer risk biomarkers, dietary intake, and physical activity. We aim to produce long-term weight loss maintenance, associated biomarker modulation, and improved quality of life in a cost-effective way that can be extended to hard-to-reach rural survivors.

Complete the Streets 3 Ways: Relationships with Physical Activity and BMI

Barbara B. Brown, PhD; Carol M. Werner, PhD; Harvey J. Miller, PhD; Ken R. Smith, PhD; Calvin Tribby; Austin Strebel

We will evaluate an impending "Complete Street" intervention that will add a new light rail line, a bike path, and a multiuse trail to neighborhoods at high risk for obesity. The intervention will transform a distinctly pedestrian unfriendly street between downtown and the Salt Lake City airport. This work will extend our past research on how walkability and transit use relate to physical activity and BMI (body mass index). In an earlier study of a new light rail stop, rail ridership increased from 50% pre-construction to 68% post-construction among nearby residents.[1] Furthermore, rail rides were associated with an increase in post-construction accelerometer-measured Moderate to Vigorous Physical Activity (MVPA) bouts. Rail riders had lower measured obesity rates, stronger place attachments and neighborhood satisfaction, stronger pro-transit development attitudes, and more objectively rated walkability on their home block.[1-4] New riders reported fewer car trips, suggesting a shift toward active transportation.[3] Results from that study converge with our county-wide studies linking walkability[5, 6] and rail stop proximity[5] to lower BMI.

The study has two major components comprising four aims. In Aim 1, structured observations test for increased use of the Complete Street elements, relative to Adjacent Streets and a Similar Traffic Street without rail/bike/trail elements. In Aims 2, 3, and 4, nearby residents are recruited to assess the social, behavioral, and health-related changes associated with the intervention. We will compare residents living close to (intervention group) and far from (control group) the Complete Streets intervention before and after construction. Residents will be measured for BMI (height & weight), wear accelerometers and GPS units for one-week pre- and post-Complete Streets construction, and complete surveys for socioeconomic, attitudinal and behavioral data. We also assess two levels of walkability. Micro-level audits will assess environmental walkability features that invite use, such as attractive destinations, well-connected streets, and cues of safety, using the Irvine-Minnesota Inventory[7]. Macro GIS walkability will assess density, diversity and pedestrian friendly design. We will examine effects at Time 1 (pre-construction), Time 2 (post-construction) and Time 3 (follow-up). Based on our prior evidence,[1, 3-6, 8-11] we hypothesize these effects, net of controls:

Aim 1. The Complete Street intervention relates to an increase in observed transit riders, cyclists, and pedestrians, compared to control streets from Time 1 to Times 2 and 3.

Aim 2. Living close to the Complete Street intervention relates to bigger Time 1 to Time 2 increases in active use of the Complete Streets (e.g., walking, bicycling) compared to living far from it.

Aim 3. Audited and resident-perceived walkability and pro-neighborhood attitudes relate to greater use of the Complete Street area, both cross-sectionally and from Time 1 to Time 2. A secondary analysis will test whether perceived crime dampens female use.

Aim 4. Users of Complete Streets will demonstrate healthier changes in Moderate to Vigorous Physical Activity (MVPA from Time 1 to 2), BMI and obesity status (Times 1, 2, & 3) compared to non-users.

The proposal offers several innovations. We target a rich 3-mode Complete Streets intervention as opposed to a single mode street improvement. We provide rare pre- post-tests of a Complete Streets intervention with appropriate control groups to assess changes in use by nearby residents and others. We employ GPS and accelerometers to measure precisely the places and times of healthy activity associated with Complete Street use by nearby residents. We examine whether this activity relates to environmental walkability and to short- and long-term obesity measures. Finally, we address active living policies--Complete Streets, zoning, walkability standards, etc.-- by linking MVPA and BMI to four modifiable environmental elements—rail, bicycle path, multi-use trail, and neighborhood walkability.

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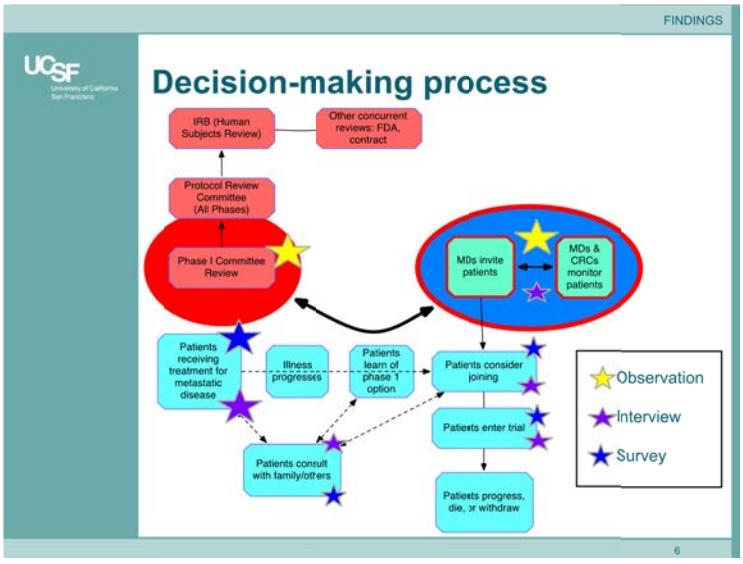
The Cancer Patient Deliberation Study: A Contextualized Analysis of Decision-Making in Early Phase Clinical Trials

Daniel Dohan, PhD; Nina Laven, PhD; Laura Dunn, MD; Christopher Daugherty, MD; Laura Trupin, MPH; Michele Bondi, MPH; Matthew Wenger, MD; Pamela Munster, MD

Background: Advances in basic and translational research may herald the arrival of new, targeted therapies that will improve cancer treatment and reduce mortality, but all of these therapies must be tested for safety in early phase (EP) clinical trials. Recruiting more patients to EP trials may speed the development of new cancer therapies, but those who participate in early phase trials – advanced cancer patients who have run out of standard therapeutic options – are a highly vulnerable population. This study uses highly-contextualized data to examine how patients with advanced cancer make decisions about participating in early phase clinical trials, including how they learn about such trials. We focus on how patients and providers jointly shape decision-making processes.

Methods: Ethnographic study at an academic cancer center. Data sources include focus groups and in-depth interviews with providers; observation of provider meetings and clinic interactions; in-depth interviews and surveys conducted at multiple points in time with a cohort of 150 patients with advanced cancer; interviews with a patient family member or other caregiver; and information from patient medical records. Qualitative data analysis is carried out using Atlas.ti software which links all data sources; quantitative analysis of survey data will be carried out using Stata software using appropriate longitudinal methods.

Results: Data sources and collection is shown in the figure. Results to date suggest that collecting qualitative and quantitative data from multiple sources in a longitudinal fashion is feasible, and we are currently developing data management and linking procedures to facilitate analyses of multiple sources of qualitative and quantitative data. Preliminary analyses of qualitative data has focused on clinician- investigators' role in the fielding and recruiting for EP trials. Clinician-investigators perceive a variety of potential benefits of EP trials: 1) Clinical: In interviews, clinician-investigators stated that some EP trials, especially of targeted agents, could lead to remission. Discussion of positive responses were common at practice meetings. 2) Emotional: In interviews, all but one clinician-investigator said discussing EP trials helped foster hopefulness when treating patients with poor or terminal prognoses. 3) Scientific: In most practice meetings and interviews, clinician-investigators discussed how conducting EP trials advanced medical science. 4) Professional: In some practice meetings and in one interview, clinician-investigators discussed how conducting EP trials can enhance clinician-investigators' careers and provide financial support for the academic center and EP program. In interviews, clinician-investigators said they discussed clinical, emotional, and scientific benefits of EP trials with patients. They did not report discussing professional benefits with patients, but in practice meetings they occasionally debated whether this topic should be part of the informed consent process. Our data also suggest clinician-investigators remain cautious about a number of issues related to the emerging science of targeted therapies including: 1) how to interpret adverse events in the context of targeted therapy trials; 2) concerns about the durability of response; and 3) questions about appropriate inclusion criteria and recruitment methods.



Conclusions: The study demonstrates the feasibility of conducting highly-contextualized analyses of patient decision-making regarding participation in EP clinical trials. Our results highlight the complexity and contingencies involved in clinician-investigators' assessment of which trials might be appropriate and suitable for which patients. We expect future results to shed further light on patients' decision-making processes and highlight ways to improve trials' processes in EP studies.

Screening for Colorectal Cancer for Average Risk Adults: Comparative Effectiveness Research on Prevention and Screening

Robert H. Fletcher, MD; Douglas A. Corley, MD, PhD; Theodore R. Levin, MD; Ann G. Zauber, PhD

Background: Screening is an established approach for reducing death from colorectal cancer. There are several currently available screening tests and strategies for colorectal cancer; each unique in its complexity, cost, potential complications and the strength of evidence supporting its use in clinical practice. These features of colorectal cancer screening complicate informed decision-making for patients, clinicians and policy makers. For instance, there is currently only limited evidence of the effectiveness of colonoscopy for cancers in the right colon. Despite these unanswered questions about its effectiveness in community settings, colonoscopy is increasingly used for screening, while tests with proven efficacy, such as sigmoidoscopy and fecal-based tests, are now less frequently used.

Aims: The specific aim of the research program is to estimate the effectiveness of screening colonoscopy in reducing death from colorectal cancer for average risk adults when compared to no screening. Of particular interest is to determine if colonoscopy is effective in reducing death from right-sided colon cancers and to examine the impact of quality of colonoscopy on its effectiveness.

Design: Nested case-control study

Setting: Persons receiving care at Kaiser Permanente in Northern California or Atlanta, GA, or Fallon Community Health Plan/Fallon Clinic.

Population and Patient: The underlying population for the study is men and women who were 55-85 years of age as of a reference date, members of the participating health plans between January 1, 2009 and December 31, 2014. Cases (n=1,200) are patients who died between 2009 and 2014 from adenocarcinoma of the colon/rectum as the immediate or underlying cause; and enrolled in the health plan for a minimum of 5 years prior to the date of CRC diagnosis (reference date). Each case will be matched to 2 controls on age, sex, length of membership in the health plan and medical catchment area.

Exposure: Screening colonoscopy determined through adjudicated review of information about reasons for screening. Data will be collected on other CRC screening tests.

Outcome: CRC-specific mortality.

Data Collection: A distributed computer program and structured medical audits collect data from several linked sources of information including medical records, electronic clinical and administrative databases, tumor registries, US census data, and vital status files. Patient interviews will be conducted on a subsample for an ancillary project.

Challenges: Key issues concerning colorectal cancer screening comparative effectiveness research are: 1) methodological challenges with using observational data; 2) integrating prevention research from bench to the community; 3) developing better risk stratification approaches; and 4) the disconnect between health care policies, clinical practice, patient and provider preferences and scientific evidence.

Does Opening a Full-Service Grocery in a Food Desert Improve Dietary Behaviors Among Low-Income African Americans?

Tamara Dubowitz, ScD; Elizabeth Steiner, MPP; Shannah Tharp-Taylor, PhD; Bonnie Ghosh-Dastidar, PhD; Rebecca Collins, PhD; Stephen Matthews, PhD; Steven Cummins, PhD; Shannon Zenk, PhD; Lisa A Bodnar, PhD; Deborah Cohen, MD, MPH

Obesity poses a serious threat to the health of our nation. Two thirds of adults in the United States are either overweight or obese, and low-income and racial/ethnic minorities are disproportionately affected. Poor dietary quality and patterns are key risk factors for obesity, and both diet and obesity are established risk factors for cancer and other chronic diseases. Increasing evidence suggests that modifying the food environment to support healthy eating may have a sustainable population impact on diet and obesity. Yet, environmental approaches are understudied.

In November of 2011, an 8.5 million dollar full-service grocery store, financed with public and private funds, will change the food retail landscape of the Hill District, a collection of contiguous neighborhoods of Pittsburgh, Pennsylvania. This joint public-private endeavor provides a unique and critically timed opportunity to examine how change in the availability of healthy foods affects food purchasing and dietary intake of residents in a US community. This full-service grocery store will be the first in nearly 30 years for this low-income, predominantly African-American community. This study capitalizes on this natural experiment. Our specific aims are (1) to describe the availability, price, and shelf-space of healthy and less healthy options within food retail venues before and after the introduction of a full-service grocery store; (2) to determine the impact of the introduction of a full-service grocery store on food purchasing behaviors and dietary intake; and (3) to determine the extent to which these associations are modified by access factors (e.g., means of transportation and degree of spatial proximity to the grocery store) and socio-cultural factors (e.g., attitudes toward eating a healthy diet, perceived barriers to eating a healthy diet, and social support for healthy eating).

We are using a matched quasi-experimental design involving one pre- and one post-"intervention" assessments of 1,000 households in the Hill District and 650 households in matched comparison neighborhood. Using door-to-door surveys, we are collecting information on participants' household food purchasing and individual dietary intake. We are also conducting pre- and post- assessments of the food environment in the intervention and comparison neighborhoods. The food environment assessments will document the number and type of food purchasing venues and assess availability, quality, and price of healthy foods in these venues. Collectively, these data will allow us to examine how opening a full-service grocery store in a low-income, predominantly African American neighborhood, affects peoples' diet and food purchasing behaviors in both the short and long term. Our study will fill significant gaps in the literature on environmental determinants of diet and obesity and will help address key policy questions about the effects of the physical environment on these outcomes.

ABC: Antidepressants and Tamoxifen Breast Cancer Pharmacoepidemiology

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In 2010, we began a large cohort study to examine the risk of subsequent breast cancer in women exposed to a potentially adverse drug interaction, tamoxifen and antidepressants (R01CA136743A2). The study includes more than 17,000 breast cancer survivors diagnosed with Stage 0 - II cancer and treated with tamoxifen from 1996 to 2007, and followed through 2009. We assembled the cohort using SEER-affiliated cancer registries from two of the largest health plans in the U.S., Kaiser Permanente Southern and Northern California. Leveraging electronic medical records, we constructed pharmacy utilization histories and followed women a maximum of 13 years. We present early results of one of the main outcomes, rates of second primary tumors in the opposite breast, according to different antidepressant use categories.

Primary Aim: Despite tamoxifen's success in reducing the risk of breast cancer recurrence, notable side effects include hot flashes and night sweats. Antidepressants have been used to relieve some of these symptoms by hundreds of thousands of breast cancer survivors. However, laboratory studies suggest that selective serotonin reuptake inhibitors antidepressants (SSRIs, e.g., paroxetine, fluoxetine) may interfere with tamoxifen's effectiveness. Tamoxifen reduces the risk of contralateral (opposite) breast cancer, but also offers protections against second primary cancers of other anatomic sites (e.g., ovarian cancer). Our study examines whether concomitant tamoxifen and antidepressant use among women diagnosed with a first primary breast cancer is associated with an increased risk of second primary tumors (i.e. independent lesions unrelated to the metastasis of the original breast cancer in the contralateral breast or other anatomic sites.)

Methods: We assembled a cohort of 8,132 women who were diagnosed with their first primary breast cancer (Stage 0 – II) from 1996 to 2007 and treated with tamoxifen and followed through 12/31/09 at Kaiser Permanente Southern California. We collected demographic, tumor, pharmacy and cancer treatment information from electronic health records and the KPSC-SEER affiliated tumor registry. The outcome measure was risk of second primary tumors identified from the tumor registry. The main independent variables were type of antidepressant (paroxetine, fluoxetine, other SSRIs, tricyclics, and others) and fraction of overlap treatment times when both tamoxifen and antidepressant treatments were prescribed (categorized in quartiles). Adjusted hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox regression models. Women were followed through second primary cancer, health plan disenrollment, death or study's end, whichever occurred first. We adjusted for age; stage and year of diagnosis; race/ethnicity; comorbidity; primary cancer treatments; aromatase inhibitor and bisphosphonate use. We repeated the Cox analysis among the subset of women who had a high tamoxifen adherence as determined by the medication possession ratio (MPR). The 80% MPR is a recognized level that suggests fairly continuous medication usage.

Preliminary Results: A total of 711 (9%) breast cancer survivors developed a second primary tumor, of which 234 (3%) were second primaries in the opposite breast. Roughly 50% (n=4,030) of the cohort used antidepressants. Of these 4,030 women, 23% (n=928) used SSRIs only. Among women with high tamoxifen adherence, women who used fluoxetine were 68% more likely to develop a second primary tumor in the opposite breast compared to those who did not use antidepressants (the reference group), but the confidence interval was wide and based on small numbers (HR=1.68, 95% CI: 0.91-3.08). When we combined outcomes (second primary in opposite breast or other anatomic site), women were 46% more likely to develop a second primary tumor (HR=1.46, 95% CI=1.04-2.06). When considering fraction of overlapping tamoxifen and flouxetine treatment time, we did not see a trend of increased risk by overlapping treatment times for the single or

combined outcome (P for trend>0.05). In addition, we found little evidence of an association with paroxetine or other SSRIs.

Discussion: Results suggest that concomitant use of fluoxetine and tamoxifen is related to an increased risk of second primary tumors of the opposite breast or other anatomic sites. However, these associations were not observed when we examined the risk by fraction of overlapping treatments as numbers were small and results were not statistically significant.

Future Steps: Next steps include expanding the analysis to include an additional 9,000 breast cancer survivors from Kaiser Permanente Northern California to confirm these results. We will carry out similar analyses to investigate possible tamoxifen-antidepressant interaction for recurrent breast cancer. We will also investigate the impact of other commonly used medications on subsequent breast cancer and mortality.

Ancillary Studies: In our presentation, we will also describe ancillary analyses that were conducted using this large and comprehensive dataset. Combined data from the two sites total over 17,000 women with Stage 0-II breast cancer treated with tamoxifen. Studies planned to date include: a) determining survival disparities among women by race/ethnicity and molecular breast cancer subtypes, b) developing a computer algorithm to derive TNM staging from EOD variables spanning across multiple years, and c) identifying recurrences through a combination of electronic utilization, diagnoses, and pathology databases.

Married Couples' Reasons for Failing to Screen for Skin Cancer

Carolyn Heckman, PhD; Susan Darlow, PhD; Teja Munshi, BDD, MPH; Sharon Manne, PhD

Skin cancer is the most common cancer in the US, and incidence continues to increase. Studies have shown that screening is helpful in detecting skin cancer at an earlier more treatable stage and can be done by oneself, with the assistance of a close other, or by a health professional. Many people fail to screen for skin cancer.

The purpose of this study was to examine screening rates in married couples, as well as the reasons for failing to screen. Participants were recruited and assessed by KnowledgePanel® from Knowledge Networks (http://www.knowledgenetworks.com/). This is a probability-based panel of potential participants for online surveys, designed to be representative of the US population. Married individuals over 50 years of age with another person living in the home were invited to participate. Participants completed an online survey in which both husbands and wives were asked to indicate whether they received a skin exam from a clinician, or performed a skin exam themselves or with the assistance of a partner. If they answered in the negative, they were asked to endorse reasons for failing to screen from a provided list and could write in other reasons. This questionnaire was completed as part of larger study examining other cancer screening behaviors.

The questionnaire was completed by 3,048 husbands and 2,942 wives (a 77% response rate). Within husbands, 39% reported receiving a clinical skin exam, while 35% of wives reported doing so. Regarding a self- or partner-assisted skin exam, 47% of husbands reported doing so, as opposed to 49% of wives. Forty-eight percent of couples matched in terms of both failing to receive a clinical skin exam, 28% did not match (i.e., one spouse had an exam, while the other did not), and 25% matched in terms of both having had a clinical skin exam. For self- or partner-assisted skin exam, 40% of married couples matched in terms of neither having an exam, 21% did not match (i.e., one spouse performed an exam, while the other did not), and 39% matched in terms of both partners performing a self- or partner-assisted skin exam.

The most commonly endorsed reason among both husbands and wives for failing to obtain a skin exam by a clinician and also not screening oneself is that a doctor did not recommend one, followed by not having any noticeable symptoms of skin cancer, and not perceiving oneself as at risk for skin cancer. Kappa coefficients were calculated to assess husbands' and wives' agreement on the reasons endorsed. Husbands and wives reached moderate agreement for the following reasons for not obtaining a clinical skin exam: healthcare provider hadn't recommended, exam would be inconvenient, did not have noticeable symptoms of skin cancer, would rather have a partner do the exam, and not perceiving oneself as at risk for skin cancer. Similar reasons for not conducting a self- or partner-assisted exam were endorsed and had similar levels of agreement (other than preferring a partner exam), though husbands and wives also had moderate agreement for not conducting an exam due to being too busy.

Results show that more than half of individuals over age 50 do not receive clinical or partner skin exams. Most couples matched in terms of both either having or not having had a skin exam and also endorsed similar reasons for not being screened. Based on these similarities and spousal influence on one another, intervening with couples as a unit may be beneficial in increasing skin cancer screening rates. Findings also highlight the role health professionals may play in encouraging screening for skin cancer, as the most highly cited reason for not getting screened is lack of recommendation from a healthcare provider. Finally, results suggest opportunities for education regarding "symptoms of" and risks for skin cancer and the fact that skin cancer may be asymptomatic.

Geographic Variation in Physician Response to a Major Chemotherapy Reimbursement Change with Implications for SEER-Medicare

Mireille Jacobson, PhD; Craig C. Earle, MD, MSc, FRCPC; Joseph P. Newhouse, PhD

Background: On January 1, 2005, Medicare instituted the average sales price (ASP) payment system for Part-B drugs, setting reimbursement at the national average of manufacturers' sales prices from two quarters prior, plus a 6 percent margin. This reduced profit margins substantially for many chemotherapy drugs. In prior work, we demonstrated that physicians responded to this change by increasing the likelihood of chemotherapy treatment for lung cancer patients.

Objectives: To evaluate geographic variation in the response to this payment change. To explore the implications of this variation for analysis using SEER-Medicare data, which covers nine states in their entirety and parts of three other states.

Research Design: We compared across state differences in changes in chemotherapy treatment for lung cancer following the payment reform. We analyzed the probability of chemotherapy treatment overall and by setting, adjusted for age, sex, race, comorbid conditions, and metastasis.

Results: Based on the national population, lung cancer patients were about 10 percent more likely to receive chemotherapy after the payment reform, with the increase concentrated in office-based oncologists. The response varied markedly across states, with treatment even declining in a few states. At the high end, the increase among states in the top decile of population was almost 30 percent. SEER is overrepresented by states with limited responses to the payment change: over 50 percent of the national cohort in SEER areas are in the bottom three deciles of the response to the treatment change and less than 10 percent is in the top population decile.

Conclusions: A large literature has demonstrated geographic variation in the level of medical spending across areas. This work demonstrates that geographic variation is also important in terms of response to policy change. This variation has important and overlooked implications for SEER-Medicare, the gold stand for cancer-related health services research. In the current context, SEER-Medicare under-represents the national response to a major chemotherapy payment reform. Despite its wealth of clinical detail, SEER-Medicare should be used with caution to evaluate national changes to the financing and organization of cancer care.

Decision Aid to Technologically Enhance Shared Decision Making (DATES)

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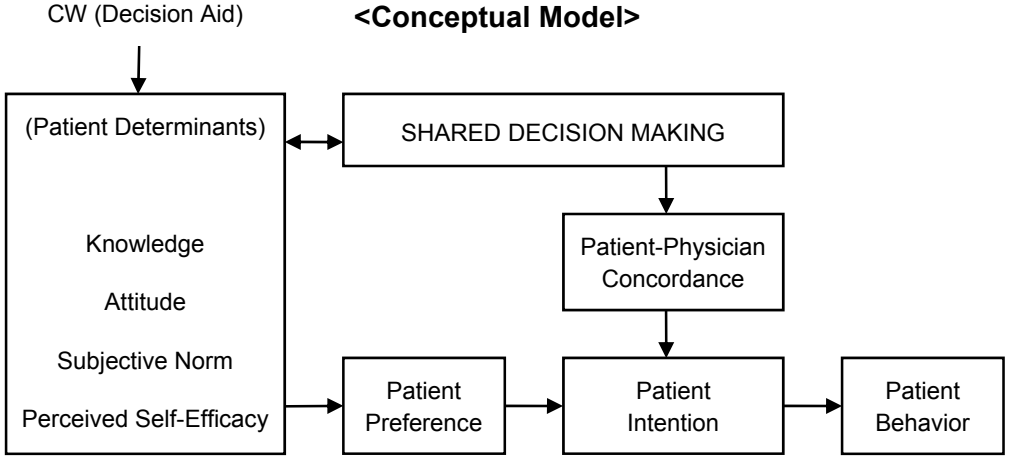
Purpose: A decision aid (DA) that clarifies patient preferences and improves decision quality could aid shared decision making (SDM) and be effective at increasing colorectal cancer screening (CRCS) rates. However, exactly how such DA improves SDM is not clear. This 4-year study seeks to provide detailed understanding of how an interactive DA affects patient-physician communication and SDM, and ultimately CRCS adherence. This presentation will review the conceptual model, design and measures of the study for feedback.

Method: This two-armed randomized controlled trial (300 patients per arm) will compare Colorectal Web (CW), the interactive DA, to a non-interactive control website in ten practices in Metro Detroit. Patients will be adults aged 50 years and over, not current on CRCS and scheduled for check-up or chronic care visit with their physician. In the clinic before the patient-physician encounter, participants will complete a Patient Baseline Survey. They will be randomized to CW or the control website. Data will be collected after the patient reviews the respective website (Post-Intervention Survey), during the patient-physician encounter (digital audio recording) and after it (Post-Encounter Survey). Chart audit will be performed six months after the encounter to determine whether the patient underwent CRCS.

Result: Primary analysis will measure the impact of CW on patient uptake of CRCS, on patient determinants/preference/intention before the patient- physician encounter, and on SDM, concordance and patient intention during and after the patient-physician encounter. Secondary analysis will employ a Structural Equation Modeling approach to understand the mechanism of the causal pathway and test the validity of our proposed conceptual model, which weaves together the components from the Theory of Planned Behavior and SDM. The goal of this presentation is to gather expert feedback on the conceptual model, study design, intervention and analysis plan to further strengthen the study.

Conclusion: The results of our study will be among the first to examine the effect of a real-time preference assessment exercise on CRCS and mediators, and, in doing so, will shed light on the patient-physician communication and SDM "black box" that currently exists between the delivery of DAs to patients and the subsequent patient behavior. Obtaining expert feedback to further refine the study would increase the validity and feasibility of the study.



New Statistical Methods for Complex Problems in Nested Case-Control Studies

Mengling Liu, PhD

The nested case-control (NCC) design is a very popular cost-effective sampling method to study the relationship between a disease and its risk factors in epidemiologic studies. NCC data are commonly analyzed using Thomas' partial likelihood approach under Cox's proportional hazards model with constant covariate effects. However, new challenges continue to arise in analysis of NCC data as modern biomedical researches are evolving and progressing, which urge the need for developing new and flexible statistical methods. Here, one of our primary goals is to study the potential time-varying effects of covariates in NCC studies. We proposed an estimation approach based on a kernel-weighted local partial likelihood and established the asymptotic properties of the proposed estimator. We further proposed a novel numerical approach to construct simultaneous confidence bands for time-varying coefficients and developed a hypothesis testing procedure to detect time-varying coefficients. The proposed method was applied to an NCC study of breast cancer in the New York University Women's Health Study. Other on-going researches include: (i) Develop partial linear estimation in NCC studies; (ii) Study NCC data with a cure fraction; (iii) Accommodate population heterogeneity in NCC studies from multiple parent cohorts using group LASSO. Our researches are supported by the NIH grants RO1 CA140632 & RO3 CA153083.

Molecular Pathological Epidemiology of Cancer: Towards Personalized Medicine, Prevention and Public Health

Shuji Ogino, MD, PhD, MS(Epidemiology)

Background: Cancer in any one organ system (e.g., colon) is not a single disease entity, but rather a heterogeneous group of diseases with different sets of genetic and epigenetic alterations. Thus, it is clear that we cannot achieve personalized cancer medicine, unless we go beyond organ-based classification into molecular classification. Each individual tumor has its own unique set of genomic and epigenomic features, and interacts with its host, which possesses a unique set of characteristics (e.g. hormones, metabolism, diet, lifestyle, and environmental exposures). To better understand the carcinogenic process and tumor progression, we have been studying interactive effects of somatic molecular changes and host factors (dietary, lifestyle and genetic factors). These new research efforts represent evolving interdisciplinary science, "***Molecular Pathological Epidemiology*** *(MPE)*" [*Ogino et al. J Natl Cancer Inst 2010; Ogino et al. Gut 2011; Ogino et al. Nat Rev Clin Oncol 2011*].

Objective: Alterations of WNT and CTNNB1 (β-catenin) signaling play roles in carcinogenesis and metabolic diseases. Given the dual roles of WNT-CTNNB1 signaling in cancer and metabolic diseases, we hypothesized interactive effects of CTNNB1 and host energy balance status on tumor cell behavior. Specifically, CTNNB1 activation might confer cancer cells autonomy from host energy balance status, while CTNNB1-inactive cancer cells might depend on patient energy balance for progression [*Morikawa et al. JAMA 2011*].

Design: We utilized MPE design, investigating interactive effects of tumor and lifestyle factors (physical activity and body mass index, BMI) on tumor behavior. We evaluated CTNNB1 localization by immunohistochemistry in 955 colon and rectal cancers. We utilized a database of two U.S. nationwide prospective cohort studies, the Nurses' Health Study (N=121,701 women followed since 1976) and the Health Professionals Follow-up Study (N=51,529 men followed since 1986). Cox proportional hazards model was used to compute multivariate mortality hazard ratio (HR), adjusting for demographic, clinical and other tumor characteristics.

Results: Among nuclear CTNNB1-negative patients, obesity (BMI ≥30 kg/m^2) was associated with significantly worse cancer-specific survival (adjusted HR=1.83; 95% CI, 1.20-2.77), while there was no association of obesity with worse survival among nuclear CTNNB1-positive cases. This finding indicated a significant tumor (CTNNB1)-host (BMI) interaction ($P_{interaction}$=0.0003). Among nuclear CTNNB1-negative stage I-III patients, post-diagnosis physical activity was associated with better cancer-specific survival [adjusted HR=0.33; 95% CI, 0.13-0.81; ≥18 vs. <18 MET (metabolic equivalent task) hours/week] while physical activity was not associated with survival among nuclear CTNNB1-positive stage I-III patients (adjusted HR=1.07; 95% CI, 0.50-2.30; ≥18 vs. <18 MET hours/week). There was a significant interaction between physical activity and tumor CTNNB1 status ($P_{interaction}$=0.046) [*Morikawa et al. JAMA 2011*].

Conclusions: This Molecular Pathological Epidemiology (MPE) study showed that post-diagnosis physical activity appeared to confer better cancer-specific survival among patients with nuclear CTNNB1-inactive tumors, but not among patients with CTNNB1-active tumors. Our novel MPE data support a role of host-tumor interactions which influence tumor aggressiveness, and may have substantial public health implications because physical activity is a modifiable lifestyle intervention. MPE research may help us achieve our goal of personalizing lifestyle and pharmacological interventions for disease prevention and treatment [*Ogino et al. J Natl Cancer Inst 2010; Ogino et al. Gut 2011; Morikawa et al. JAMA 2011; Ogino et al. Nat Rev Clin Oncol 2011*].

Effectiveness of Preoperative MRI in Breast Cancer Surgery and Outcomes

Tracy Onega, PhD; Anna Tosteson, ScD; Rebecca Hubbard, PhD; Beth Virnig, PhD, MPH; Karla Kerlikowske, MD, MPH; Diana Buist, PhD; Rob Gutierrez, MD

Breast magnetic resonance imaging (MRI) has been used for preoperative evaluation in women with breast cancer for almost two decades, but is still the subject of clinical controversy. While preoperative breast MRI is known to detect additional cancer, the impact of this on preoperative work-up, surgical treatment and outcomes is not clear. A major question is whether detecting additional cancer leads to more aggressive work-up and surgery (mastectomy instead of breast conserving surgery) without any concomitant benefits. Prior studies have not compared *population-based* use of breast MRI with standard imaging modalities in relation to breast cancer surgery and important outcomes, such as re-excision, subsequent tumors, and mortality. Expanding use of breast MRI necessitates a large-scale assessment of these outcomes to inform clinical practice guidelines and to understand potential benefits and harms for women with breast cancer. This proposed research will: 1) examine the influence of preoperative breast MRI on additional cancer detection, preoperative work-ups and the relation with mastectomy vs. breast conserving surgery; 2) compare breast MRI with mammography ± ultrasound in relation to re-excision, subsequent tumor events, and mortality; 3) assess utilization of preoperative breast MRI nationally and in subgroups of women, such as those with increased breast cancer risk; 4) estimate population-wide impacts of preoperative breast MRI use through Markov models of utilization and outcomes. We will use newly established linkages of the national Breast Cancer Surveillance Consortium (BCSC) registry data with Medicare and Group Health claims data to address these aims in a unique and novel way. These data will leverage existing resources by augmenting health care utilization data with risk factor, comorbidity, clinical assessment, and pathology information. The BCSC data consists of a large population of women primarily from community settings, enabling us to examine subgroups of women, such as those with ductal carcinoma *in situ*, dense breasts or family history of breast cancer, and to have greater generalizabilty than previous studies. Our overall objective is to provide critical evidence about the effectiveness of preoperative breast MRI compared to standard imaging modalities to inform current practice protocols, women's decision-making, and health care policies. In this era of new technologies and health care reform, identifying *if* and *when* advanced modalities benefit patients is of the utmost importance to both patients and resource allocation efforts.

Genome-Wide Analysis of Renal Cancer Risk and Survival

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Renal cell carcinoma (RCC) is the 8th most common cancer in the US and the 10th most common form of cancer death, with over 34,000 cases and 12,000 deaths each year. A sharp increase in the incidence of RCC was observed in recent decades with some of the greatest increases happening in Central Europe and among the black population in the US. Apart from smoking, obesity and hypertension, much of the etiology of this disease remains to be identified. There is increasing evidence that genetic factors influence susceptibility to RCC, although this hypothesis has been understudied.

Resulting from an IARC/US NCI collaboration, a joint European/US genome-wide association (GWA) study has recently been conducted to identify new loci associated with RCC risk, involving approximately 3,800 RCC cases (1,000 from cohort studies) and 8,500 controls (3,700 from cohort studies). Results point to two loci that are genome-wide significant, as well as a third locus with very suggestive results, and suggest new causal pathways for RCC.

To accelerate our understanding of the mechanisms underlying RCC, we plan to extend this study by incorporating an additional 3,800 cases and 4,800 controls from a series of population-based case-control and cohort studies from Europe, the US, and Australia. Inclusion of cohort studies has been facilitated via the NCI Cohort Consortium.

In addition to its size, our study will be unique in several ways: (1) extensive clinicopathological information and survival of cases will be collected; (2) genome-wide analyses for the association between genetic variants and RCC will be conducted for both disease onset and survival; (3) a comprehensive biorepository of germline DNA and tumor DNA and RNA on at least 2,000 cases will be developed; (4) whole-genome gene expression profiling on fresh renal tissue and tumor tissue will be obtained to complement results obtained from the germline genotyping analyses.

An Investigation of AURKA- and PTPRJ-Interacting Human Colorectal Cancer Susceptibility Loci

Madelyn M. Gerber, BS; Nathan P. Schultz, BS; Mehmet Deveci, BS; Heather Hampel, MS; Umit Catalyurek, PhD; Amanda Ewart Toland, PhD

In 2010, an estimated 51,370 deaths occurred in the United States due to colorectal cancer (CRC). Inheritance of low-penetrance susceptibility genes contributes to CRC risk. Linkage and functional analyses using crosses between cancer-resistant and cancer-susceptible mouse strains identified *Aurora A kinase* (*Aurka*) and *Protein tyrosine phosphatase receptor type J* (*Ptprj*) as two strong candidate cancer susceptibility genes shown to interact synergistically with other loci to increase cancer susceptibility. We hypothesize that the risk associated with these two genes in humans is dependent on alleles at interacting loci. We furthermore propose that CRC susceptibility alleles will show preferential copy number gains and resistance alleles will show preferential copy number losses in human colon tumors. To test these hypotheses, we first identified a set of candidate genes from interacting *Aurka* and *Ptprj* loci by comparing RNA-Seq data from CRC-resistant and CRC-susceptible mouse strains for differences in potentially functional SNPs, mRNA expression, or splicing. We chose 295 SNPs for preferential allelic imbalance studies from these candidate genes, along with SNPs from genome-wide association studies and from gene-gene interaction studies. SNPs chosen for analysis were those that tagged genes, were associated with eQTLs and/or were potentially functional. Using Sequenom MassARRAY iPLEX Gold genotyping, we quantitatively genotyped the 295 SNPs in 200 normal/tumor DNA pairs from CRC cases enriched for microsatellite stability for allelic specific imbalance. Among the genotyped SNPs, 25 exhibited statistically significant preferential allelic imbalance (p-value < 0.05), with the most significant mapping to *MCC* (rs11955699; p-value = 0.0004), *FBXO11* (rs2537742, p-value = 0.001), *SNX10* (rs2699814, p-value = 0.004), and the *AURKA* 3' untranslated region (rs8173, p-value = 0.005). We are currently validating these SNPs in a replication sample set. Confirmed variants will be further validated, tested for function using *in vitro* studies, and assessed for cancer risk.

Alcohol Use and Smoking Cessation Rates of NY Quitline Callers

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Objective: Based on published data showing that daily smokers have high rates of hazardous drinking and higher rates of smoking relapse, we hypothesized that New York State Smokers' Quitline (NYSSQL) callers would exhibit elevated rates of risky drinking and risky drinking callers would report lower rates of smoking cessation.

Methods: We assessed rates of hazardous drinking among 88,479 callers to the NYSSQL using both AUDIT-C and NIAAA guidelines. Using 2 routine NYSSQL 2-week follow-up interviews (n=14,123 & n=24,579) and a 3-month follow-up interview (n=2,833), we also compared smoking cessation rates for callers who met criteria for hazardous drinking compared to moderate drinkers and non-drinkers.

Results: At baseline, 55.8% of callers reported drinking, 38.9% reported hazardous drinking by AUDIT-C, and 22.9% reported hazardous drinking by NIAAA guidelines. Hazardous drinkers (as defined by NIAAA) did not differ from non-drinkers but had lower smoking cessation rates than moderate drinkers for the standard 2-week follow-up [adjusted OR (95% CI)=1.17 (1.07, 1.29), p=0.001], the "Enhanced Services Program" 2-week follow-up for uninsured callers [adjusted OR (95% CI)=1.09 (1.01, 1.17), p=0.04], and the 3-month follow-up [adjusted OR (95% CI)=1.23 (0.98, 1.55), p=0.07].

Conclusions: High rates of hazardous drinking exist among smokers calling the NYSSQL, and these hazardous drinking callers had lower smoking cessation rates compared to moderate drinking callers. Given that quitlines have the potential to reach large numbers of smokers, tobacco quitlines may provide a venue for providing brief alcohol intervention to these high risk drinkers. Future studies should evaluate whether a brief alcohol intervention would result in improved smoking cessation rates for hazardous drinking smokers.

This research was supported in part by National Institutes of Health grants R01-CA140256, R21-CA127818, K12-DA000167, and by a contract from the New York State Department of Health.

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Genetic Determinants of Expression Phenotypes in Aggressive Prostate Cancer

Liang Wang, MD, PhD; Hui Tang, PhD; James Cerhan, MD, PhD; Stephen Thibodeau, PhD

Although less common, aggressive prostate cancer (PC) is clinically more significant, accounting for more than 27,000 deaths in the US annually. Thus, understanding the genetic mechanism underlying the aggressive phenotype will have a significant impact on prevention strategies, prognosis and potentially targeted therapy. To identify genes and genetic variants critical to aggressive phenotype of PC, we examined lymphoblastoid cell lines derived from 125 PC patients using combination of eQTL mapping and network analysis. We identified a highly co-expressed gene module that is not only enriched for genes known to play critical roles in cell cycle regulation (false discovery rate = 3.50E-50) but is also significantly correlated with the aggressive phenotype (p=3.67E-11). From this module, we further defined 20 hub genes that were highly connected to other genes. Association study in the hub genes revealed significant association of 9 cis-eSNPs (7 genes) with the aggressive PC. Finally, we integrated eQTLs into a directed graphic model to infer causal network. We observed significant causal relationship in multiple genes. The most obvious causal interaction is rs11752161→*TTK*→trait (LEO score=0.97). Interestingly, the rs11752161 also showed association with *TTK* expression (*cis*-eQTL p=0.0052) and with aggressive PC (genetic association p=0.007). These results strongly suggest that the rs11752161 may increase risk of aggressive PC via regulating *TTK* expression, and demonstrate the power and efficiency of a joint modeling of the eQTLs, eSNPs, and clinical phenotype.

Self-Administered Acupressure for Treatment of Persistent Cancer-Related Fatigue (PCRF)

Ananda Sen, PhD; Sara Al-rawi, ND, MPH; Gary Merel; Brodie Burris; Richard Harris, PhD

Purpose: Persistent cancer related fatigue (PCRF) is a common symptom experienced by many cancer survivors. PCRF is currently under-diagnosed, with between 20% to >60% of survivors experiencing fatigue. There are few effective treatment options for these patients. Acupressure offers a potential low-toxicity treatment option for PCRF.

Methods: We performed a pilot trial of acupressure in cancer survivors experiencing moderate to severe PCRF. Potential participants were excluded if they had other causes of fatigue such as anemia, malnutrition, or chronic fatigue syndrome. Participants were randomized to one of three treatment groups: relaxation acupressure (RA), high intensity stimulatory acupressure (HIS), and low intensity stimulatory acupressure (LIS). Participants performed acupressure for 12 weeks between 3 to 14 times per week, depending on group. Change in fatigue was our primary outcome. Secondary outcomes were assessment of blinding and compliance to treatment. The effect of group on Brief Fatigue Inventory (BFI) was assessed with mixed method regression.

Results: Fatigue was significantly reduced across all treatment groups (mean±SD reduction in BFI: RA 4.0±1.5, HIS 2.2±1.6, LIS 2.7±2.2; p =0.027), with greater reductions in the relaxation acupressure group. In an adjusted analysis the group difference remained significant after controlling for age, cancer type, cancer stage, and cancer treatments (p=0.013). Across all groups, greater time spent performing acupressure was associated with greater reductions in fatigue (r=-0.39; p=0.037). Participants were blinded to treatment groups (p=0.62).

Conclusions: Self-administered RA engendered greater reductions in fatigue when compared to either HIS or LIS acupressure. Across groups, these reductions in fatigue were on the order of 45% to 70%, which were clinically relevant and as such could represent a viable alternative for cancer survivors with PCRF.

Designing Regional Surveillance to Inform Local Cancer Control: The California Health Interview Survey (CHIS)

Nancy Breen, PhD; Alyssa Grauman, MPH

CHIS, the largest state health survey in the United States, produces comprehensive, population-based health data from the most racially, ethnically, and linguistically diverse state in the U.S. The CHIS Governing Board consists of key CHIS stakeholders and is led by the University of California at Los Angeles (UCLA) Center for Health Policy Research.

First fielded in 2001, CHIS is a continuous telephone survey that provides data from households selected from all 58 California counties. Estimates can be made for adults, adolescents, and children for 41 of the 58 individual counties. CHIS is culturally adapted for California's diverse populations and is conducted in five languages: Spanish, Chinese (Cantonese and Mandarin), Vietnamese, and Korean.

The National Cancer Institute (NCI) supports CHIS to provide public use cancer control data for racial-ethnic minority groups not available on other surveys and to understand how cancer affects people throughout California. NCI has sponsored cancer control items on CHIS since its inception. Previous cancer control topics include screening (breast, lung, colorectal, prostate, cervical), family history of cancer, the human papillomavirus (HPV) vaccine, and health behaviors influencing cancer risk.

CHIS data can provide evidence to help improve access to care, build healthier communities, better serve ethnic communities, and support vital research on health outcomes, health policies, and health disparities.
For more information about CHIS, visit http://appliedresearch.cancer.gov/surveys/chis/.

Health Disparities Calculator (HD*Calc)

Nancy Breen, PhD; Stephen Meersman, PhD; Antoinette Percy-Laurry, MSPH

The Health Disparities Calculator (HD*Calc) is statistical software designed to generate multiple summary measures to evaluate and monitor health disparities (HD). HD*Calc was created as an extension of SEER*Stat that allows the user to import SEER data or other population-based health data and calculate any of eleven disparity measurements.

HD*Calc allows researchers to select and apply a range of health disparities measures to their data. HD*Calc was developed to expand the range of measures for evaluating health disparities related to cancer and can be used with any dataset in any research arena. Cross-sectional and trend data (e.g., cancer rates, survival, stage at diagnosis) categorized by disparity groups (e.g., area-socioeconomic status, race/ethnicity, geographic areas) can be imported into HD*Calc to generate four absolute and seven relative measures of disparity. The results are displayed as tables and charts, which may be exported for use in other applications.

HD*Calc can be used to:

- Quickly and accurately compare different measures of disparities by various social and economic determinants of health such as race/ethnicity, education, socioeconomic status, and geographic area;
- Evaluate multiple summary measures for monitoring and presenting health disparities;
- Graphically explore underlying trends in data; and
- Easily export tables and graphs.

The HD*Calc tool and all training resources are available at: http://seer.cancer.gov/hdcalc/.

Informatics for Consumer Health (ICH): Innovation through Sharing, Funding, and Dialog

Health Communication & Informatics Research Branch, Behavioral Research Program, Division of Cancer Control & Population Sciences, National Cancer Institute; Westat

Consumer health information technology (IT) applications hold great promise for encouraging and supporting behavior change and improving health outcomes across the health care spectrum. Technologies such as patient reminder systems, secure messaging systems between patients and providers, in-home monitoring tools, patient education systems, pharmaceutical error-checking routines, and enhanced decision support tools for self-care have already resulted in improved outcomes and reduced costs. Recognizing the need to bring together diverse health IT stakeholders to stimulate the development and integration of evidence-based tools and commercial products, a collaboration of Federal partners convened the "Informatics for Consumer Health: Summit on Communication, Collaboration, and Quality" in 2009. To extend the work begun by the summit, *InformaticsForConsumerHealth.org* was launched in 2010. Developed and maintained by the DCCPS Behavioral Research Program, the website aims to bridge the gap between healthcare and IT by providing a knowledge base and platform for conversation to foster collaborations and partnerships among public and private stakeholders.

What can this site do for you? If your interests are in ICH, this website provides you with *current* information about the latest conferences, workshops, webinars, and other events; a database of peer-reviewed journal articles showcasing *current* research; and a listing of opportunities for funding and collaboration. The site also features an interactive blog where experts representing the range of stakeholders can share their perspectives on *current* successes, trends, and challenges in the field of ICH. Conversations extend to social media platforms, including a LinkedIn group with over 300 members and a Twitter account with 150 followers. With the website established and its core users engaged, DCCPS will continue efforts to raise the profile of the site by expanding its reach to stakeholders and leveraging the resources of Federal partners to cross-promote activities and initiatives relevant to ICH.

This information can assist you in developing grant applications that meet the research objectives of the National Cancer Institute and the Office of the National Coordinator for health care delivery systems. Specifically, the website can provide information to assist in your development of behavioral research and evidence-based tools and products that can:

- Improve the safety and efficiency of health care and reduce health disparities
- Improve the coordination of care
- Engage patients and families as active participants in their health care
- Improve population and public health
- Ensure adequate privacy and security protections
- Diffuse technology-based health interventions
- Deliver applications to people regardless of location

Cancer Control Items on the National Health Interview Survey

Carrie Klabunde, PhD; Alyssa Grauman, MPH

The National Health Interview Survey (www.cdc.gov/nchs/nhis.htm), sponsored by the National Center for Health Statistics (NCHS), is the principal source of information on the health of the U.S. civilian, non-institutionalized household population. Each year, approximately 35,000 households participate in the survey. Conducted in person, the NHIS is regarded as the 'gold standard' for nationally-representative, population-based, self-reported health data in the U.S. NCI has collaborated with NCHS to field cancer control questions on the NHIS since 1987. The most recent Cancer Control Supplement to the NHIS was conducted in 2010; these data are now publicly available. The 2010 NHIS Cancer Control Supplement covered the following topics:

- Diet, nutrition, and physical activity
- Cancer screening (breast, cervical, colorectal, prostate, and lung)
- Sun safety/sun protection
- Tobacco use and control
- Genetic testing
- Medication use (e.g., tamoxifen; raloxifene)
- Family history of cancer
- Cancer risk assessment
- Cancer survivorship

NHIS questionnaire items and datasets are used extensively to address a variety of cancer-related research questions. More than 300 papers using NHIS cancer control data have been published: http://appliedresearch.cancer.gov/cgi-bin-pubsearch/pubsearch/index.pl?initiative=NHIS.

NHIS will field a new Cancer Control Supplement in 2015, and an interim data collection on cancer screening in 2018. These data will be important for future research as well as for assessing national progress toward meeting Healthy People 2020 cancer control targets, and informing goal-setting for Healthy People 2030.

Tobacco Use Supplement to the Current Population Survey (TUS-CPS)

Anne Hartman, MS, MA; Sonja Stringer, MPH

The Tobacco Use Supplement to the Current Population Survey (TUS-CPS) is a National Cancer Institute (NCI) survey of tobacco use and policy information that has been administered triennially as part of the U.S. Census Bureau's and Bureau of Labor Statistics' Current Population Survey since 1992, most recently in 2010-2011. The Centers for Disease Control and Prevention (CDC) has co-sponsored a few survey periods. TUS-CPS data are available for public use. Because it uses a large, nationally representative sample, the TUS-CPS is a key source of national, state, and local-level data on smoking, other tobacco use, and policy. It contains information on approximately 240,000 individuals within a given survey period. Researchers can use the data to monitor progress in the control of tobacco use, conduct tobacco-related research, evaluate tobacco control programs, and examine tobacco-use-related health disparities. A unique feature is the ability to link the TUS-CPS to social, economic and other risk factor data from the Census Bureau and Bureau of Labor Statistics and its supplements and to cancer incidence and cause-specific mortality data from the National Longitudinal Mortality Study.

The National Cancer Institute Consortium of Cohorts

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The NCI's Cohort Consortium is an international collaborative infrastructure designed to serve as a research resource providing data and biospecimens to study gene-gene and gene-environment interaction in the etiology of cancer. The mission of the Cohort Consortium is to foster communication among investigators leading cohort studies of cancer; promote collaborative research projects for topics not easily addressed in a single study and identify common challenges and solutions in cohort research.

Consortium membership includes cohorts with large numbers of cancer cases for whom there had been prospective biospecimen collection as well as other epidemiologic cohorts interested in large-scale collaborative research projects, with a minimum of 10,000 participants and with some data on risk factors. 41 cohorts have joined the Consortium, involving over 4 million people. The member cohorts are national and international in scope, covering large and diverse populations. There are several investigations nested in the Cohort Consortium resulting in high impact publications. Examples of such are the Breast and Prostate Cancer Cohort Consortium, BMI Pooling Project and Pancreatic Cancer Cohort Consortium.

Cancer Post Genome-Wide Association Studies (GWAS) Initiative: International Collaborative Studies of Breast, Colon, Lung, Ovarian and Prostate Cancers

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Genome-wide association studies (GWAS) provide the initial evidence that a particular genetic region harbors a cancer susceptibility locus. However, further research is needed to identify causal variant(s) and understand the biology of complex diseases. The National Cancer Institute Post-GWAS Initiative solicited applications proposing collaborative and transdisciplinary research projects addressing two overall goals: 1) To pursue promising scientific leads from previously generated GWAS of cancer and 2) To coordinate and accelerate integrative post-GWAS discovery research, which could provide the basis for expediting clinical translation and public health dissemination of the findings.

To achieve these two overarching goals, the site-specific projects are structured into three components: 1) Discovery and replication: finding of new associations through pooled analyses, independent replication of associations and fine mapping of association signals, 2) Biological studies: identification of risk-modifying variants, determination of biological mechanism of risk-enhancement and examination of functional consequences of variant, and 3) Epidemiology: evaluation of gene-gene and gene-environment interactions, assessment of penetrance and population attributable risk and development of complex risk models and evaluation of their clinical validity. The Initiative also expands the power of GWAS to minority populations, thereby increasing our understanding of racial and ethnic disparities in health. Descriptive data for the ongoing projects are presented. The participating cooperative agreements are: Discovery, Biology, and Risk of Inherited Variants in Breast Cancer (DRIVE), Elucidating Loci Involved in Prostate Cancer Susceptibility (ELLIPSE), Follow-up of Ovarian Cancer Genetic Association and Interaction Studies (FOCI), Transdisciplinary Research in Cancer of the Lung (TRICL), and ColoRectal Transdisciplinary Study (CORECT).

Four working groups were formed to facilitate collaborations and methods sharing across studies: 1) Analytic and Risk Modeling, to develop analytic tools, share analytic approaches, develop and validate models to characterize risk factors for cancer 2) Epidemiology and Clinical, to assist in the overall plans for collaborative epidemiologic analysis, such as looking at pan-cancer genes or pathways common to many cancers and the use of standard control sets across consortia. This group also focuses on the examination of genetic determinants of aggressive cancer/metastasis across cancers. 3) Functional Assays, to share approaches to the characterization of functional consequences of risk variants, and identify specific gene targets and their interaction mechanism. This group recently published in *Nature Genetics* on the "Principles for the post-GWAS functional characterization of cancer risk loci" (PMID: 21614091) 4) Next-Generation Genomic Technologies, to evaluate current and emerging technologies and platforms for optimal genotyping and sequencing, and assist in the search for less common and rare variants.

As a result of this work, the Initiative will have contributed to the progress of knowledge beyond association of a region with cancer risk towards causality. The assembly of very large and well characterized populations by the site-specific investigative groups will provide the ideal material for future in-depth characterization of genetic and environmental susceptibility to cancer. The Initiative is open to collaboration with the scientific community at large. Further information is available at http://epi.grants.cancer.gov/pgwas/.

Capturing Symptom Burden and Treatment Tolerability in Cancer Clinical Trials: Patient-Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE)

Sandra Mitchell, PhD, CRNO, AOCN

The standard lexicon for reporting adverse events in National Cancer Institute sponsored clinical trials is the Common Terminology Criteria for Adverse Events (CTCAE). Currently, adverse events are reported by clinicians, yet evidence suggests that compared to patient-report, clinicians may underestimate symptom severity and onset. An interdisciplinary research team identified CTCAE items with a subjective component amenable to patient reporting. Published literature and existing self-report measures were examined. Systematic review of CTCAE identified 81 symptoms amenable to patient reporting; however items were unsuitable for patient-report due to intermingling of symptom attributes (severity, interference) within items and technical jargon. Based on review of the literature, the symptom attributes to be measured included amount/frequency, severity, and interference with usual activities. A recall period of 7 days was selected and standardized response options were formulated. The items were refined through cognitive interviewing. A web-based interface was developed to administer the items, and allows clinicians to customize surveys, set up e-mail alerts for missed surveys or concerning symptoms, and generate reports. Validity, usability, and scalability of the PRO-CTCAE prototype are currently being tested in academic and community-based settings. Language translations and an interactive voice-response mode are in development. PRO-CTCAE is designed to improve the accuracy, precision, and validity of adverse event reporting in cancer clinical trials. Simultaneously, it offers an efficient data collection routine that may yield new insights into the symptom experience and strengthen patient engagement in symptom self-management.

Grid-Enabled Measures (GEM): A Tool to Facilitate the Use of Shared Measures and Harmonized Data

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Currently there is little coordination of scientific measures and data sets in most health sciences. The Grid Enabled Measures (GEM) portal (https://www.gem-beta.org/) is a decision support tool which uses technology mediated social participation to create and support a virtual community of health scientists. GEM portal has two over-arching goals: 1) To provide an interactive online system that enables users to search for, share, download, and vet health-related research measures that are tied to theoretically-based constructs; and 2) to facilitate the sharing (i.e., uploading and downloading) of harmonized data, resulting from the use of common measures. This promotion of shared measures and harmonized data will facilitate the initiation of more efficient and powerful studies and 'prospective meta-analyses', resulting in a coordinated and more efficient research enterprise to ultimately improve health and well-being.

Advancing Scientific Progress: Genomic Data Sharing and Access Through dbGaP

Stefanie Nelson, PhD; Laura Buccini, DrPh, MPH; Barbara Guest, MSW, MPH

The NIH's Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS) (NOT-OD-07-088) was developed to balance protection of participant privacy and confidentially with broad sharing of data to rapidly advance research to identify common genetic factors that influence health and disease. This policy calls for all investigators receiving NIH funds to submit their data to the NIH Database of Genotypes and Phenotypes (dbGaP) and allow its use by the scientific community. The guiding principle of the NIH's data sharing policy states:

> *"The greatest public benefit will be realized if data from GWAS are made available, under terms and conditions consistent with the informed consent provided by individual participants, in a timely manner to the largest possible number of investigators."*

dbGaP is an NIH-sponsored data repository designed to archive and distribute the results of NIH-funded studies investigating interactions between genotypes and phenotypes; dbGaP also houses data generated by non-NIH funded studies, which are considered for inclusion in dbGaP on a case-by-case basis. Currently, dbGaP contains over 1,900 datasets from 149 studies covering a broad range of phenotypes and disease states. Data housed in dbGaP is available to eligible investigators through a controlled access process. Investigators may use dbGaP datasets for original discovery-based research and also for development of methods related to analysis of genomic data and its application to health-related issues. Each Institute that funds GWAS has a Data Access Committee that is responsible for reviewing requests for data and granting (or denying) access. Access has been granted to more than 1,700 approved users from more than 150 institutions, both U.S. and international. The success of dbGaP as a resource for the scientific community can be judged by the number of peer-reviewed publications and presentations that have used dbGaP data—more than 600 at the time of this writing.

Using SEER-Medicare Data for Cancer-Related Health Services Research

Joan Warren, PhD; Helen Parsons, MPH

The SEER-Medicare data result from the linkage of two large, population-based resources. Sponsored by the National Cancer Institute, the Surveillance, Epidemiology, and End Results (SEER) Program collects information on cancer incidence, prevalence and survival from more than 18 geographic areas representing 28 percent of the US population. SEER routinely collects data on patient demographics, primary tumor site, stage at diagnosis, first course of treatment and follow-up for vital status. For Medicare-eligible individuals with cancer, the SEER-Medicare files include all Medicare claims for covered health care services from the time of a person's Medicare eligibility until death.

The linkage of these two data sources results in a unique source of information that can be used for an array of epidemiological and health services research. For example, investigators using this dataset have conducted studies on patterns of care along the cancer continuum, following individuals prior to diagnosis through death. Examples of studies include identifying patterns of treatments, surveillance and end-of-life care for persons with cancer in the Medicare population. Investigators have also examined the use of cancer tests, technology adoption and trends in the cost of cancer care.

Diet and Physical Activity Research Resources of the Risk Factor Monitoring and Methods Branch

Jill Reedy, PhD, MPH, RD; Amy Subar, PhD, MPH, RD; James McClain, PhD, MPH

The Applied Research Program's Risk Factor Monitoring and Methods Branch (RFMMB) contributes to reducing cancer in the U.S. by serving as a critical link between etiologic research on cancer risk factors, such as diet and physical activity, and the translation of such research into targeted and effective interventions for prevention.

Dietary research resources supported by RFMMB include:

- Usual intake estimation
- Healthy Eating Index (HEI)-2005
- National Health and Nutrition Examination Survey (NHANES) Dietary Web Tutorial
- Web-Based Automated Self-Administered 24-Hour Dietary Recall (ASA24)
- Glycemic Index (GI) Values Database
- Measures of the Food Environment (MFE) Web Site
- Dietary Assessment Calibration/Validation (DACV) Register
- Short Dietary Assessment Instruments
- Diet History Questionnaire (DHQ)

Physical activity research resources supported by RFMMB include:

- Activity monitor SAS programs
- Metabolic Equivalent (MET) Values for activities in the American Time Use Survey (ATUS)
- Standardized Questionnaires of Walking and Bicycling Database

Information about all of these resources is available on the RFMMB website at http://riskfactor.cancer.gov.

Applied Research Program Mission and Research Resources

Susan Scott, MPH

The Applied Research Program (ARP) mission is to:

- Understand how and why cancer care and control activities in the United States influence patterns of care and trends in cancer incidence, morbidity, mortality, and survival
- Support methodologic research to improve survey data collection and clinical databases, develop assessment tools for use in clinical trials and observational studies, and analyze existing cancer control data
- These data are used to evaluate patterns and trends in cancer-associated health behaviors and risk factors, health care services, economics, and outcomes

ARP research networks:

- HMO Cancer Research Network (CRN)
- Cancer Care Outcomes Research and Surveillance Consortium (CanCORS)
- Breast Cancer Surveillance Consortium (BCSC)
- International Cancer Screening Network (ICSN)

Publicly available data resources supported by ARP include:

- National Health Interview Survey (NHIS)
- California Health Interview Survey (CHIS)
- Tobacco Use Supplement to the Current Population Survey (TUS-CPS)

ARP-supported tools for researchers include the following, plus many others:

- Automated Self-Administered 24-hour Dietary Recall (ASA24)
- Usual Dietary Intake Estimation
- Measures of the Food Environment
- National Provider Surveys of Cancer-Related Practices
- Patterns of Care/Quality of Care (POC/QOC) Studies
- SEER-Medicare Data Linkage
- SEER-Medicare Health Outcomes Survey (SEER-MHOS) Data Linkage
- Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

ARP funding opportunities focus on:

- Building capacity for cancer control surveillance research
- Investigating health behaviors and health services
- Determining the impact of health behaviors and services on cancer burden
- Developing new methods for measuring health behaviors, risk factors, and care delivery options

For more information, please visit http://appliedresearch.cancer.gov