Heterogeneity and Variation in Body Mass Index in the Framingham Heart Study Offspring Cohort Over 37 Years

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**Background:** The rapid trajectory of average weight in the US has implicated changing environmental or neighborhood factors as possible contributing factors. Using longitudinal data from the Framingham Heart Study (FHS) Offspring Cohort over 37 years, we examined trends in BMI accounting for residential mobility to determine variation in BMI at the individual and neighborhood levels over time.

**Methods:** Subjects were examined up to eight times through 2008. We excluded observations with missing body mass index, smoking status, alcohol intake or census tract of residence and when a subject was living in a nursing home or the age of a subject was less than 21 years. The final sample size was 4,148 subjects with 27,133 observations. We used gender-stratified, cross-classified multilevel models to account for time-varying attributes of individuals and residential neighborhoods (census tracts) with measured BMI as the outcome, controlling for individual demographics and behaviors and neighborhood poverty. We included a random slope for linear time at the individual level to account for heterogeneity in BMI trajectories between individuals.

**Results:** Mean BMI increased from 24.0 kg/m\(^2\) at Wave 1 to 27.7 at Wave 8 for women and from 26.6 to 29.0 for men. The proportion of the total BMI variance explained by the individual level, the intraclass correlation coefficient (ICC), was high, 0.88 for women and 0.86 for women, meaning that the individual level explained 88% and 86% of all variation in BMI. Inclusion of the individual-level covariates did not appreciably change the ICCs, explaining less than 10% of the individual-level variance for women and none of the variance for men. Neighborhood-level variance contributed minimally to BMI variance. Large individual-level random slopes demonstrated that the variance in BMI increased significantly over time for both men and women (Figure 1). Covariates that were positively associated with BMI for men and women were increasing age, alcohol consumption, a high school education, being married, and being employed. Smoking was negatively associated. Neighborhood poverty was not significantly associated with BMI.

**Conclusions:** Unmeasured individual factors explained almost all of the variation in BMI over nearly 40 years, and BMI variance increased substantially over time. The limited relationship of the neighborhood of residence to BMI variation over time suggests that neighborhood-level interventions may have an overall limited impact on weight.
Electronic Health Record Tool Reduces Antibiotic Use: The integrated Clinical Prediction Rules (iCPR) Trial

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**Background:** Clinical decision supports (CDS) have been developed as platforms within electronic health records (EHRs) to help introduce evidence-based medicine (EBM) into routine care. Clinical prediction rules (CPRs) are frontline decision aids that combine evidence with real-time patient history, exam, and laboratory data. Despite being well-validated EBM tools, CPRs have been underutilized in practice. Previous studies of CDS for upper respiratory infections (URIs) have demonstrated negative results with utilization rates as low as 6%. We have developed an Integrated Clinical Prediction Rules Clinical Decision Support system (iCPR) that incorporates two well-validated URI CPRs (Walsh Streptococcal Pharyngitis and Heckerling Pneumonia CPRs) into the most widely used commercial outpatient EHR system (EpicCare™). Our study is a randomized controlled trial of the effectiveness of the iCPR tool in changing provider antibiotics and diagnostic test ordering behaviors for URI’s within an urban ambulatory primary care practice that uses a large commercial EHR system.

**Methods:** The study setting was a large ambulatory academic primary care practice. All primary care providers (140 residents and faculty) were recruited for participation. Consenting providers were randomized in a 1:1 fashion into intervention or control. After a brief training, intervention providers had the iCPR tool activated in their EHR profile. The intervention consisted of an optional EHR embedded CDS that triggered from specific complaints, diagnoses, and/or orders relevant to strep or pneumonia placed at the point-of-care. The interface then guided risk stratification and facilitated antibiotic orders, notes, supportive therapies, and patient instructions. The primary outcome was the difference in antibiotics ordered for step or pneumonia during encounters between intervention and control providers after one year. Secondary outcomes included differences in diagnostic test ordering between groups and use of each component of the iCPR tool among intervention providers. Generalized estimating equations were used to test for differences in antibiotic utilization among groups accounting for clustering by provider.

**Results:** Over 1 year, enrolled providers conducted 1007 (586 intervention, 421 control) encounters that triggered the iCPR tool, representing 3% of all their encounters during this period. More than half (63%) of the encounters seen by providers enrolled in the intervention arm launched the risk stratification tool and 58% utilized the bundled iCPR interface associated ordering option. We observed a 40% reduction in the likelihood of antibiotic ordering in intervention versus control encounters (30% vs. 39%, OR: 0.6 [0.5-0.9], p=.01). Chest x-rays for pneumonia were ordered in 20% of control encounters and 21% of intervention encounters (OR: 0.9 [0.5-1.6], p=.70) while rapid strep tests were 30% less likely in the intervention arm (29% vs. 40%, OR: 0.7 [0.5-1.0], p=.05). Broad spectrum antibiotics were ordered less frequently amongst intervention encounters (71% vs. 77%, OR: 0.75 [0.44-1.31], p=0.31).

**Conclusions:** The iCPR randomized control study demonstrated significant reductions in antibiotic and some diagnostic test ordering. Moreover, the tool was frequently used by providers; a significant improvement over previous CDS studies for URIs. These data suggest that EHR embedded CPRs have the potential to enhance the implementation of EBM in primary care and improve quality.
**Arrow Plots: An Innovative Method Of Plotting Surrogate And Clinical Outcomes In Meta-Analyses**

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**Background:** Meta-analyses of health care interventions usually study dichotomous patient-centered clinical outcomes such as mortality. Clinicians titrate medical therapy to a surrogate outcome that is a continuous biomarker. Forest plots in meta-analyses do not, however, show well the relation between a surrogate outcome, baseline risk, and a clinical outcome. The objective of this study is to develop a visual display of quantitative information from meta-analyses to illustrate the link between a purported biomarker, baseline risk, and clinical outcome.

**Methods:** Differences in outcomes of randomized controlled trials are plotted on two dimensions for two independent variables: changes in a clinical outcome and changes in a surrogate outcome. Arrows begin with the results of the control groups, reflecting baseline risk, and end with the results of the intervention groups. Bayesian meta-analysis is performed and impact of therapy is described with judicial analogies. We illustrate by reanalyzing 3 recent meta-analyses, intensive lowering of LDL-cholesterol (CTT 2010), intensive insulin therapy in hospitalized patients (Kansagara 2011), and intensive glucose lowering treatment in type 2 diabetes (Boussageon 2011).

**Results:** The change in the y-coordinate of each arrow indicates relative risk reduction. The slopes of the arrows represent the relation between change in the biomarker and change in the clinical outcome. For intensive lowering of LDL-cholesterol (Figure), arrows are homogeneous suggesting a consistent association between biomarker and clinical outcome. For diabetes in hospitalized patients, arrows are heterogeneous suggesting inconsistent association between biomarker and outcome. However, two visually identifiable regions suggest association between biomarker and outcome in subpopulations. Intervention may improve clinical outcome in subpopulations with very high baseline glucose or very high baseline risk of mortality. For intensive glucose lowering in type 2 diabetes, arrows are heterogeneous without forming any identifiable homogeneous regions suggesting inconsistent association between biomarker and outcome.

**Conclusions:** This data visualization is innovative because two independent variables are dimensioned and Bayesian analyses of regions facilitate interpretation. Arrow plots allow assessment of biomarkers as indicators of therapy response and influence of baseline risk. Further research should develop a statistical measure for homogeneity of slopes of arrows and a method of identifying the thresholds of biomarker and baseline risks that separate benefit from harm.
Novel “tobacco” product use and association with smoking cessation: a national study

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Background: Since 2006, the major US cigarette manufacturers acquired smokeless tobacco companies and have begun selling smokeless tobacco products bearing cigarette brand names (e.g. Marlboro snus, Camel snus). At the same time, electronic cigarettes (e-cigarettes) have begun to be aggressively promoted on the internet as a smoking cessation device or as a way to use nicotine in smokefree environments. There is a dearth of clinical data on effect of novel tobacco product use on smoking cessation, and these products are not approved for this purpose. We examined rates of trial and current use of novel alternative tobacco products among smokers and its association with smoking cessation behavior.

Methods: A nationally representative probability-based sample of 1,836 current or recently former (quit within last two years) smokers completed an online cross sectional survey in November 2011. Current (past 30 day) and ever use of traditional smokeless tobacco (loose leaf, moist snuff), novel smokeless tobacco (snus, dissolvable), hookah, and electronic cigarettes was compared among former smokers (23.3% of sample), smokers who tried to quit in the past year (59.9%), and smokers who did not try to quit (16.8%). Comparisons between groups were made using chi-square tests for categorical variables, and multivariate logistic regression was used to evaluate the association between current alternative tobacco product use and quit attempts, controlling for age, sex, race/ethnicity and education.

Results: Overall, 44% of smokers had tried one of the novel/alternative tobacco products, and 30% of smokers expressed interest in using novel tobacco products to try to reduce their health risk, cut down, or quit smoking. Electronic cigarettes had been tried most frequently (20.4% of respondents had ever used, with 40% of ever users reporting current past month use), and dissolvable tobacco products had been tried least frequently (2.8% ever used). Males used traditional smokeless and snus tobacco products more frequently than women (p<.001); women used e-cigarettes more frequently (p<0.05), and use of hookah, and dissolvable tobacco did not differ by gender. E-cigarettes had been used significantly more frequently by smokers who tried to quit smoking but failed (22.5%), than successful quitters (17.6%) or smokers who had not tried to quit smoking (15.2%) (p=0.006). Ever using an alternative tobacco product was associated with having made a cigarette quit attempt in the past year (OR=1.47, 95%CI [1.20, 1.80]), as was current use of any product (OR=1.30 [1.06, 1.59]). Ever using an alternative tobacco product was not independently associated with successful smoking cessation.

Conclusions: Many smokers in the USA have tried novel alternative tobacco products, and e-cigarettes were tried more frequently than both the traditional and newer smokeless tobacco products like snus. New smokeless tobacco products and e-cigarettes appear to appeal more to women than traditional smokeless tobacco. Alternative tobacco product use is associated with attempting to quit smoking, but not having quit successfully. Clinicians should be aware of novel tobacco products, particularly e-cigarettes, and should screen for use among smokers, as this may indicate stronger interest in smoking cessation and an opportunity to encourage evidence-based cessation treatments.
Influence of Gender Role Attitudes In Smoking And Drinking Among Girls From Jujuy, Argentina

Raul Mejia

Background: Gender role is influenced by culture, temporal factors, traditions, expectations and assumptions. Ideas about gender roles and femininity may have a role in explaining differences in tobacco and alcohol consumption in adolescents. Objective: To evaluate the effect of gender role attitudes in smoking and drinking among mostly Indigenous girls from northwest Argentina.

Methods: Self-reported data were obtained from a 2006 survey of tenth grade female students attending a random sample of 27 urban and rural schools in Jujuy Province. Questions about tobacco smoking and alcohol consumption were adapted from global youth surveys. We also constructed a scale to assess adolescents’ perception of traditional or egalitarian sex roles based on a comprehensive literature review. In formative work, the questionnaire was reviewed by a panel of experts in gender studies and administered to 10 adolescents during in-depth interviews to evaluate comprehension and face validity. The final scale consisted of 10 items with 5-point response options of agreement-disagreement scale where 1=strongly agree to 5= strongly disagree. Factor analysis of the item data suggested a 5 item factor with a Cronbach alpha of 0.72. These items asked about women staying at home to care for children, men working to earn a living for the family, women accepting men’s decision if they disagree, women working outside the home leading to more crime by youth and the women belonging at home and not in a job. Responses to the items that minimize sexual stereotypes reflected non-traditional/egalitarian gender roles. In this study we hypothesized those girls who ascribe to more egalitarian gender roles have higher risk of ever or current smoking or drinking than those who ascribe to more traditional roles.

Results: In 2006, 2,133 girls aged 13-18 responded, 71% identified as Indigenous, 22% as mixed indigenous/European, and 7% as European. Nearly 60% were ever smokers (ever tried or experimented with cigarette smoking), 32% were current smokers (in past 30 days), 58% were ever drinkers, 27% have drunk in the previous month, and 13% were heavy drinkers (had 5 or more drinks in past month). A logistic regression model was generated for each outcome using the gender role scale as the main predictor and adjusting for known confounders from these data (having any friends who smoke, having a job, repeating a grade in school, living with both parents, living with someone who smokes at home, depressive symptoms in previous year, worked in tobacco growing and/or selling, and smoking media literacy). Gender role was positively associated with significantly increased odds of ever smoking and ever drinking, drinking in the last month and heavy drinking.

Conclusions: Girls in Jujuy who ascribe to more egalitarian gender roles have greater chances of smoking or drinking than those who ascribe to more traditional ones.