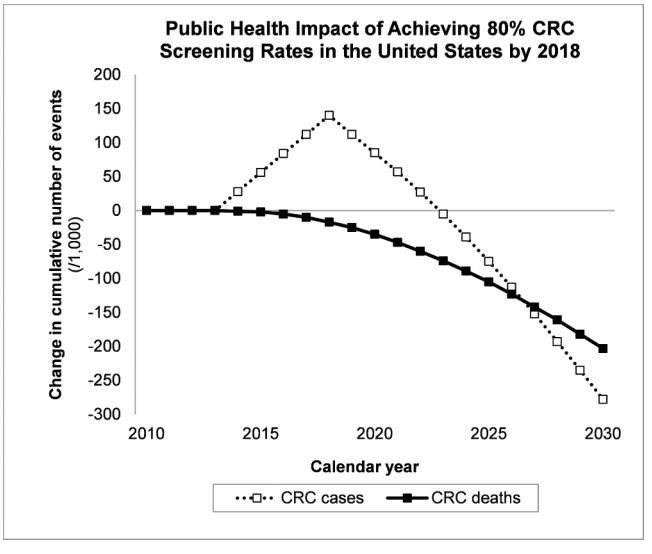
Colonoscopy Before FOBT+ Result	FOBT+ persons, No. (%) n = 40,605	CRCs, No. n = 1,655	Risk of CRC, rate per 1,000
Colonoscopy in 10 years before FOBT+	9,906 (24.4%)	143	14.4
Colonoscopy >0 to 2 yrs before FOBT+	2,960 (7.3%)	31	10.5
Colonoscopy >0 to 6 mos before FOBT+	378 (0.9%)	5	13.2
Colonoscopy >6 to 12 mos before FOBT+	698 (1.7%)	5	7.2
Colonoscopy >12 to 24 mos before FOBT+	1,884 (4.6%)	21	11.1
Colonoscopy >2 to 5 yrs before FOBT+	4,462 (11.0%)	61	13.7
Colonoscopy >5 to 10 yrs before FOBT+	2,484 (6.1%)	51	20.5
Colonoscopy >10 yrs before FOBT+ or never done	30,699 (75.6%)	1,512	49.3

969

Public Health Impact of Achieving 80% Colorectal Cancer Screening Rates in the United States by 2018

Reinier G. Meester, Chyke A. Doubeni, Ann G. Zauber, Luuk Goede, Theodore R. Levin, Douglas A. Corley, Ahmedin Jemal, Iris Lansdorp-Vogelaar

BACKGROUND: Colorectal cancer (CRC) screening is cost-effective in adults of age 50-75 years, but is currently used by only 58% of the eligible adults in the United States (US). The National Colorectal Cancer Roundtable, a national coalition of public, private and voluntary organizations, recently launched an initiative to increase US CRC screening rates to 80% by 2018. We evaluated the potential public health benefits of achieving this goal. **METHODS**: We simulated the 1980-2030 US population 50-100 years of age using microsimulation modeling (MISCAN-colon). Population estimates were obtained from the US Census Bureau, past CRC incidence and mortality estimates were based on Surveillance Epidemiology and End Results program data, and test-specific historical screening was based on 1987-2013 National Health Interview Survey data. The effects of increasing screening rates from 58% in 2013 to 80% in 2018, by screening previously unscreened adults, were compared to a scenario in which the screening rate remained at approximately 60%. We examined the influence of detection and removal of adenoma and early cancers on new CRC cases and deaths per year during short-term follow-up (to 2020) and extended follow-up (to 2030). The outcomes of interest in our analysis were cancer incidence and mortality rates, and absolute number of cancer cases and deaths. **RESULTS**: Increasing screening rates from 58% to 80% by 2018 would initially increase CRC incidence, but would subsequently reduce CRC incidence by 17% and CRC mortality by 19% during short-term follow-up (to 2020). Increasing screening uptake to 80% would reduce CRC incidence and mortality rates by a total of 22% and 33%, respectively, by 2030. The estimated effects on incidence and mortality rates would translate in approximately 43,000 new CRC cases and 21,000 CRC deaths averted per year by 2030, and a total of 278,000 cases and 203,000 deaths averted from 2013 through 2030 (**Figure**). **CONCLUSION**: Considerable reductions in CRC incidence and mortality and the avoidance of over 200,000 CRC deaths through 2030 are projected to result if the uptake of CRC screening in the US increases from the current 58% to 80% by 2018. This underscores the potential gains of public health efforts targeted to screening underutilization.



1010

Disease-Associated Enterotypes and Metabotypes in Families With Pediatric Inflammatory Bowel Disease

Jonathan P Jacobs, Maomeng Tong, Ian McHardy, Maryam Goudarzi, Paul Ruegger, Dermot McGovern, James Borneman, Albert Joseph Fornace, Marla Dubinsky, Jonathan Braun

Background: The intestinal microbiome and its metabolic products are believed to play a critical role in the pathogenesis of IBD. Existing studies of the IBD microbiome/metabolome have employed cross-sectional cohorts. We undertook a family-based study to identify microbial and metabolic features of IBD taking into account the shared environmental and genetic factors within families. **Methods:** Fecal samples (n=90) were collected from 21 pediatric IBD patients and their first-degree relatives for 16S sequencing (Illumina HiSeq) and mass spectrometry (Q-TOF Premier). The cohort included 36 individuals with IBD (21 probands, 6 siblings, 9 parents); of these, 26 had Crohn's disease. Dirichlet multinomial models were used to group individuals into enterotypes and metabotypes based upon their microbial composition and metabolomic profile. Multivariate models incorporating gender, ethnicity, mode of delivery, anti-TNF therapy, and family were used to identify OTUs and spectral features associated with enterotype/metabotype and IBD. Spectral features were grouped into modules by WCGNA. Modules associated with metabotype were identified using set enrichment analysis. **Results:** Individuals in this cohort separated into 2 enterotypes and 3 metabotypes. Enterotype and metabotype were associated with disease state ($p<10^{-6}$) and with one another. The association between enterotype and metabotype was preserved when healthy individuals were analyzed separately ($p=2x10^{-4}$). Family had a statistically significant effect on metabotype in healthy individuals (p=0.008) and may have also influenced enterotype (p=0.08). The IBD-associated enterotype had increased Lachnospiraceae (Blautia, [Ruminococcus]) and decreased Ruminococcaceae (Faecalibacterium, Ruminococcus). The two enterotypes were not distinguished by Bacteroides abundance. Prevotella overgrowth was seen in only 10% of patients. 14 metabolite modules in the positive ionization mode and 4 metabolite modules in the negative ionization mode were associated with metabotype, representing 594 spectral features (212 with FDR<0.05). In contrast, only 38 spectral features were associated with IBD status in multivariate models at FDR<0.05. Validation of putative IDs was performed for two modules, revealing reduced abundance of glutamate, tryptophan, and tyrosine in the metabotype most strongly associated with IBD and reduced valine and phenylalanine in the second IBD-associated metabotype. **Conclusion:** Individuals in families with IBD can be divided into groups with shared fecal metabolomic profiles and microbial composition, suggesting common stable host-microbiome states. The existence of these states in healthy individuals argues that they do not simply represent the effects of intestinal inflammation. Healthy individuals who have an IBD-associated metabotype and/or enterotype may be at increased risk for developing IBD.

1017

A Cystic Fibrosis Transmembrane Conductance Regulator Channel Activator, Junchoto, Improves Opioid Induced Constipation in Rats

Yumi Harada, Yayoi Saegusa, Seiichi Iizuka, kazuya Maemura, Naoki Fujitsuka, Tomohisa Hattori

Background/Aim: Use of opioid receptor stimulants for relieving pain in cancer patients is increasing, but it may induce severe chronic constipation, resulting in deteriorated quality of life of these patients. Junchoto (JCT) is a traditional Japanese Kampo medicine used empirically for chronic constipation patients. The aim of this study was to elucidate the effects of JCT on an opioid-induced constipation model and clarify the action mechanisms. **Methods:** Seven-week-old male Sprague-Dawley rats received oral administration of codeine phosphate (CPH, 12 mg/kg) to stimulate opioid receptors. JCT (300 or 1,000 mg/kg) or lubiprostone (3 μg/kg) was administered orally in the constipation model. Small bowel transit in CPH-treated rats was measured 15 min after administering JCT and CPH following fasting using 10% aqueous solution of activated charcoal. The secretion of small intestinal fluid in non-treated rats was measured 30 min after administration of lubiprostone or JCT following 24-h fasting. Response to the CIC-2 chloride ion channel was measured with the patch clamp procedure using Chinese hamster ovary cells. The cystic fibrosis transmembrane conductance regulator (CFTR) channel activity was measured with the JCT-added short-circuit current as a marker of electrogenic chloride secretion using human bronchial epithelial cells. **Results:** Administration of JCT or lubiprostone in the CPH-induced constipation model rats resulted in a significant increase in fecal count [control: 42.5 ± 1.6 (n); CPH: 22.7 ± 1, $p < 0.001$; JCT 300 mg/kg: 31.2 ± 1.6, $p < 0.05$; JCT 1,000 mg/kg: 45.2 ± 2.7, $p < 0.001$; lubiprostone: 34.7 ± 2.7, $p < 0.01$] and dried fecal weight compared to CPH group. Fecal count, dried fecal weight, and small bowel transit was markedly higher for both drugs compared to the CPH group. The secretion of small intestinal fluid was increased by JCT or lubiprostone in non-treated rats. The CFTR channel changed dose-dependently by administration of JCT (50-400 μg/mL) and a CFTR-specific inhibitor (CFTRinh-172) abolished this change. JCT had no effects on the ClC-2 chloride channel. **Conclusion:** The CFTR activator, JCT, increased fecal count and dried fecal weight in both non-treated and CPH-induced rats. JCT improves constipation by increasing secretion of small intestinal fluid, suggesting JCT has a clinical effect on opioid stimulant-induced chronic constipation via a novel mechanism in the form of CFTR activation.