Research Fellowship Scheme

F1 - Income Inequality and Cardiovascular Health in China

Dr KWOK Man-ki
School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China

Introduction and Project Objectives: Whether absolute income (income per se) or relative income (social comparisons of income) at the household or neighbourhood level affects cardiovascular disease (CVD) risk in China is understudied. Relative income have been hypothesized to affect health via material and/or psychosocial stress pathways. However, it remains unclear whether stress biomarkers, such as cortisol, are on the pathway from income to CVD risk. This project aimed to examine the associations of absolute and relative household and neighbourhood income with CVD risk, and the mediating role of cortisol, in Hong Kong Chinese, and to assess whether cortisol, a major stress hormone, plays a potential causal role in CVD and its risk factors in Westerners and Hong Kong Chinese.

Methods: Complementary designs with an observational study and two Mendelian randomization (MR) studies were used. Based on Hong Kong's FAMILY Cohort, 17,607 adults (recruited from 2009 to 2014) were included for the observational study to examine the associations of income with CVD risk, and 1,562 adults (attended clinical follow-up started in 2016) were used to assess the mediating role of cortisol and for the MR study in Hong Kong Chinese. Publicly available genome-wide association studies (GWAS) with large sample size and extensive genotyping for cortisol and CVD and its risk factors were included for the MR study in Westerners.

Results: In the observational analysis in Hong Kong Chinese, relative household income deprivation was associated with higher systolic blood pressure but lower body mass index, whereas it was unrelated to self-reported CVD and diabetes. Neighbourhood income inequality was generally unrelated to CVD risk, nor was absolute income. Cortisol did not clearly mediate the association of relative household income deprivation with systolic blood pressure. Using the MR analysis, genetically predicted cortisol was unrelated to ischemic heart disease, ischemic stroke, diabetes or other CVD risk factors in Westerners, nor CVD risk in Hong Kong Chinese.

Conclusion and/or Discussion: Relative household income deprivation was not consistently associated with cardiovascular health in Hong Kong Chinese adults, nor was neighbourhood income inequality or absolute income. Relevance of relative and absolute income to cardiovascular health may be context specific. Cortisol unlikely plays a role in cardiovascular risk, casting doubts on the cortisol-related pathway to CVD. Better understanding of complex psychosocial mechanisms and alternative mediating pathways would inform more effective preventive strategies to close the income gap in cardiovascular health in China.

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Research Fellowship Scheme

F2 - Evaluation of Uptake and Impact of Physical Activity Guidelines for Preschool Children in Hong Kong

Dr Wendy HUANG Yajun
Department of Sport, Physical Education and Health, Hong Kong Baptist University, Hong Kong SAR, China

Introduction and Project Objectives: The first guidelines for physical activity and sedentary behaviour for children aged 2 to 6 years was first released in 2012 by the Department of Health and a revised version was published in 2018. This study investigated the awareness and knowledge of the guidelines among parents and preschool teachers, examined the associations of awareness and knowledge with beliefs, intention, and children's physical activity and sedentary behaviour as suggested by health communication theory, and identified perceived barriers and facilitators to implementation and develop messages recommendations supplementing the guidelines through focus group interviews.

Methods: A complementary (quantitative and qualitative) research approach was applied. 351 children and their parents were recruited from 8 kindergartens. Children worn an activPAL accelerometer for seven consecutive days to measure physical activity and sedentary time. Parents reported their child's sedentary screen time and sociodemographic information, and responded to questions assessing their awareness, knowledge, belief and intention of the guidelines. Focus group interviews were conducted among a group of parents and teachers to gauge their feedback on the guidelines.

Results: Very few children (14.6%) met the physical activity guidelines and 41.6% of them met the screen time recommendations. Awareness and knowledge of the guidelines was low within parents. Being aware of the having better knowledge was associated with better belief of the guidelines and higher intention of the guidelines' adoption. Parents' awareness of the guidelines was positively related with children's physical activity, while better knowledge and higher intention within parents were favourably correlated with children's sedentary behaviour. Parents and teachers generally agreed with the recommendations, however, they identified various barriers for implementation. They also suggested using innovative mediums for dissemination and communication.

Conclusion and Discussion: Compliance with the PA guidelines is low for preschool children in Hong Kong. There is a lack of awareness and adequate knowledge of the physical activity guidelines among parents. The guidelines should be supplemented with clear messages catering for local needs and to ensure that precursors to behaviour change could be motivated. Certain segments of the populations should be targeted in future health promotion. Increasing stakeholders' awareness and knowledge of the guidelines may be helpful to enhancing belief and intention of adopting the guidelines.

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Research Fellowship Scheme

F3 - Establishing a Best Panel of Stool-based Detection for Non-invasive Colorectal Neoplasm Screening

Dr Jessie LIANG Qiaoyi
Research Associate Professor, Department of Medicine and Therapeutic, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

Introduction and Project Objectives: Colorectal cancer (CRC) screening can facilitate successful treatment and reduce cancer incidence. We aimed to establish stool-based multitarget tests to improve colorectal neoplasm screening by involving our previously identified CRC-associated miRNAs (reflecting changes in host cells) and bacterial markers (reflecting environmental risk factors).

Methods: Multiplex TaqMan probe-based qPCR for bacterial markers (Fusobacterium nucleatum (Fn), Bacteroides clarus (Bc), Clostridium hathewayi (Ch), a Lachnoclostridium sp. 'm3' and an undefined species 'm7') and multiplex MGB probe-based RT-qPCR for miRNAs (miR92a, miR135b, miR21, miR145 and miR133a) were established. Stool samples from 698 subjects, consisting of 203 patients with CRC, 207 patients with adenoma (120 advanced adenoma (AA) and 87 non-advanced adenoma (NAA)) and 288 normal controls, were tested. Statistical modelling to employ these markers with/without fecal immunochemical test (FIT) was conducted using logistic regression (LR), multinomial logistic regression (mLR) and random forest classification, with best subsets regression and cross validation where appropriate. Diagnostic performance of the new models were assessed.

Results: With conventional cutoff at 100 ng Hb/mL, FIT detected 72.3%, 17.9% and 0% of CRC, AA and NAA respectively although at superior specificity of 99.5%. Without FIT, combining 4Bac (Fn, m3, Bc and Ch) and 3 miRNAs (miR92a, miR145 and miR135b) by mLR model showed sensitivities of 89.9%, 44.6% and 45.6% for CRC, AA and NAA respectively at 84.8% specificity. Bacterial markers (Fn, m3, Bc, Ch) combined with FIT by LR model showed sensitivities of 94.4%, 44.1% and 38.4% for CRC, AA and NAA respectively at 84.7% specificity. miRNAs (all five) combined with FIT by LR model showed sensitivities of 90.2% for CRC and 43.3% for AA at 80.3% specificity, although not satisfactory for NAA. Models involving all three types of markers showed further improved diagnostic performances. The mLR model involving 4Bac (Fn, m3, Bc, Ch), 3 miRNAs (miR92a, miR145, miR135b) and FIT detected 96.9%, 48.2% and 43.0% of CRC, AA and NAA respectively at 84.8% specificity. The random forest classifier involving 2Bac (Fn, m3), 4 miRNAs (miR92a, miR21, miR135b, miR133a) and FIT showed sensitivities of 94.3%, 46.4% and 46.8% for CRC, AA and NAA respectively at 84.8% specificity.

Conclusion: The combination of fecal bacterial and miRNA markers increases the sensitivity for colorectal neoplasm detection, and could be easily implemented with FIT. This study provides marker panels and corresponding modelling methods, involving fecal bacterial and miRNA markers with or without FIT, for clinical implementation to improve colorectal neoplasm screening.

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Research Fellowship Scheme

F4 - The Cost-effectiveness of Prostate Health Index for Prostate Cancer Detection in Chinese Men

TEOH JY [1], LEUNG CH[1], WANG MH[2], CHIU PK[1], YEE CH[1], NG CF[1], WONG MC[2]
[1] *S.H.Ho Urology Centre, Department of Surgery, The Chinese University of Hong Kong, Hong Kong SAR, China.*
[2] *The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong SAR, China.*

Introduction and Project Objectives: Prostate-specific antigen (PSA) and prostate health index (PHI) have been used as biomarkers for prostate cancer detection. In this study, we aimed to evaluate the cost-effectiveness of PHI for prostate cancer detection in Chinese men.

Method: We developed a Markov model for Chinese male patient aged 50-75 years old. The PSA strategy was to offer TRUS-PB for all patients with elevated PSA of 4-10 ng/mL. The PHI strategy was to offer PHI for patients with elevated PSA of 4-10 ng/mL. TRUS-PB would only be offered for patients with PHI >35.0. Model inputs were extracted from local data when available. The cost per quality-adjusted life years gained for both strategies were calculated. The incremental cost-effectiveness ratios in relation to the willingness-to-pay (WTP) threshold were compared. One-way sensitivity analysis and probabilistic sensitivity analysis were performed. Cost-effectiveness acceptability curves were also constructed.

Results: With a Markov model of 25 screening cycles from age 50 to 75 years, the mean total costs per man were estimated to be USD 27,439 in the PSA strategy and USD 22,877 in the PHI strategy. The estimated effects were estimated to be 15.70 in the PSA strategy and 16.05 in the PHI strategy. The PHI strategy was associated with an expected decrease in cost of USD 4562 and an expected gain of 0.35 QALY, resulting in an ICER of USD -13056.56. The results were shown to be robust upon one-way sensitivity analysis. Upon Monte Carlo simulation, the PHI strategy was more cost-effective for 100% of the iterations. The PHI strategy demonstrated dominance over the PSA strategy regardless of what WTP threshold we use.

Conclusion: A PHI-based screening strategy may be more cost-effective than a PSA-based strategy for prostate cancer detection in Chinese men. These results support consideration of a PHI-based approach for prostate cancer in Hong Kong.

Discussion: Our study showed that the PHI strategy could reduce the need of prostate biopsy, prostate biopsy-related complications, and was much more cost-effective than the PSA strategy. The study results had huge implications in the management of patients with elevated PSA in Hong Kong. Currently, PHI has been adopted for routine use by urology specialists in the public system in Hong Kong.

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