

DCEG Studies in China

Stephen J. Chanock, M.D.

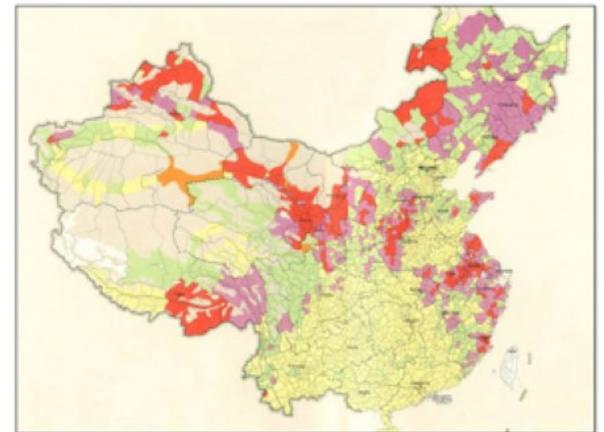
Christian C. Abnet, Ph.D.

Division of Cancer Epidemiology and Genetics

June 24, 2015

DCEG Studies in China

- More than 30 years collaboration
 - Currently over 25 studies
- Insights from cancer maps led to epidemiologic field studies
 - Unusual patterns of risk for lung, esophagus, and stomach cancer
- Unique opportunities to study occupational exposures



Chinese Collaborators



DCEG Trainees in China



DCEG Studies in China: Special Exposures

- Occupational exposures

Shanghai, Tianjin

- Benzene
- Formaldehyde
- Trichloroethylene
- Particulates: diesel exhaust and coal combustion products



- Physical activity

Shanghai

DCEG Studies in China: Lung Cancer

- Lung cancer among never-smoking women

Shanghai, Shenyang, Xuanwei

- Indoor air pollution from coal used for cooking
- Identified risks
- Intervention by ventilating stoves
- Lung cancer rates decreased substantially



- Residential radon from underground dwellings

Shenyang



Consortium to Study Environmental and Genetic Etiology of Lung Cancer in Never-Smoking Females

- Genome-wide Association Study
 - ~13,000 cases from 19 studies
- 8 Novel Signals
 - Majority unique to non-smokers
 - No association found at 15q25.1
 - 2 gene-environment interactions with indoor use of coal for heating/cooking
- Ongoing Exome Sequencing
 - Susceptibility study
 - Tumor/Normal pairs
- Link residential histories to air pollution databases and satellite data



● Study sites

Combined GWAS of Esophageal Squamous Carcinoma

- Call for Data Sharing
 - Published editorial in *Nature Genetics* 2011
 - Based 3 parallel papers for ESCC
- Pooled, combined analysis
 - Individual data exchange
 - New loci
 - Correction of 4 previously published

nature
genetics

Corrigendum: Genome-wide association analyses of esophageal squamous cell carcinoma in Chinese identify multiple susceptibility loci and gene-environment interactions

nature
genetics

Wu, et al. 46:1001-1006, 2014

Joint analysis of three genome-wide association studies of esophageal squamous cell carcinoma in Chinese populations

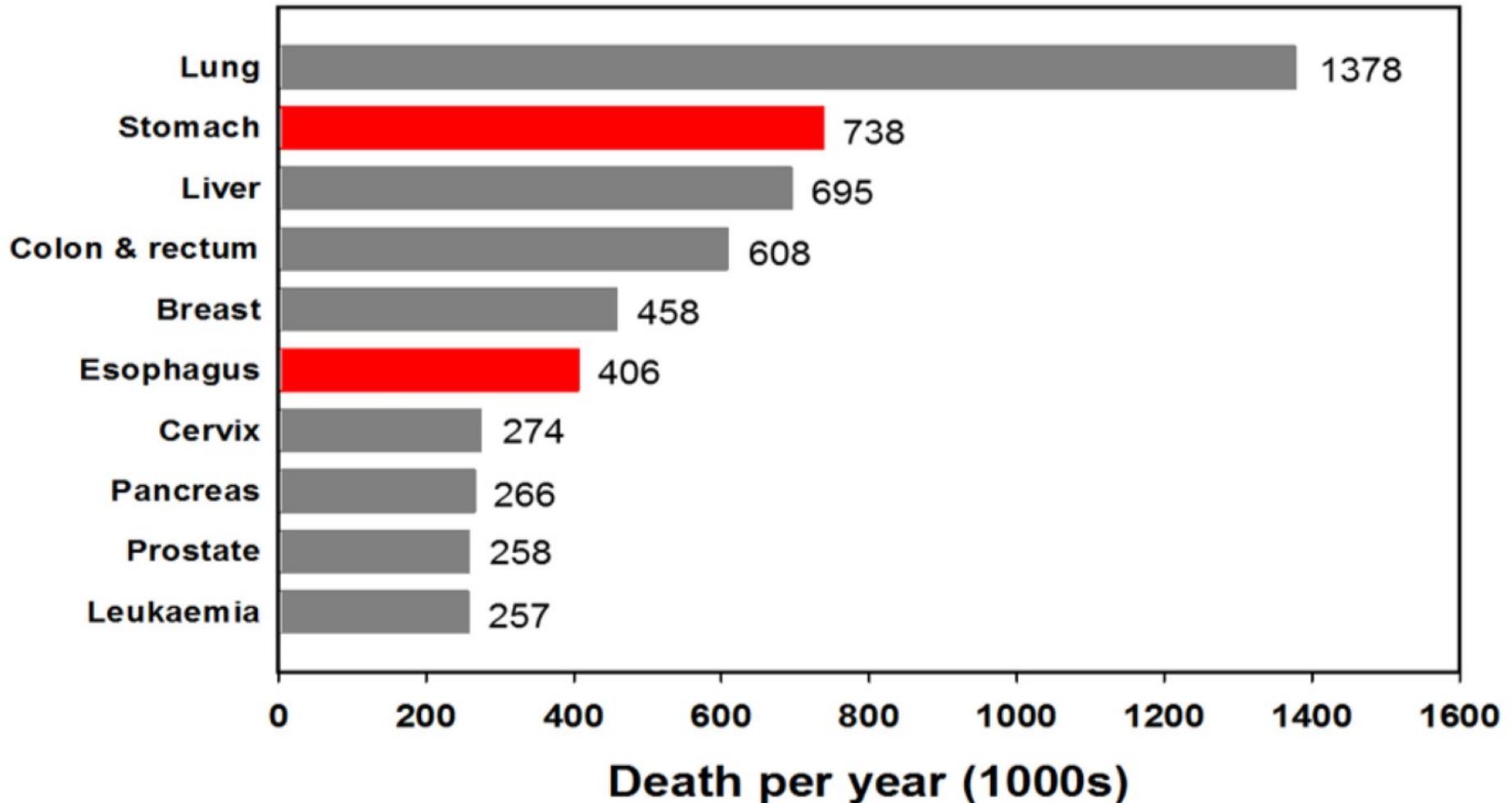
Chen Wu^{1,63}, Zhaoming Wang^{2,3,63}, Xin Song^{4,5,63}, Xiao-Shan Feng^{6,63}, Christian C Abnet^{2,63}, Jie He^{7,63}, Nan Hu^{2,63}, Xian-Bo Zuo^{8,63}, Wen Tan^{1,63}, Qimin Zhan¹, Zhibin Hu⁹, Zhonghu He¹⁰, Weihua Jia^{11,12}, Yifeng Zhou¹³, Kai Yu², Xiao-Ou Shu^{14,15}, Jian-Min Yuan¹⁶, Wei Zheng^{14,15}, Xue-Ke Zhao⁵, She-Gan Gao⁶, Zhi-Qing Yuan¹, Fu-You Zhou¹⁷, Zong-Min Fan⁵, Ji-Li Cui^{4,5}, Hong-Li Lin^{4,5}, Xue-Na Han⁵, Bei Li⁵, Xi Chen^{5,18}, Sanford M Dawsey², Linda Liao², Maxwell P Lee¹⁹, Ti Ding²⁰, You-Lin Qiao²¹, Zhihua Liu¹, Yu Liu¹, Dianke Yu¹, Jiang Chang¹, Lixuan Wei¹, Yu-Tang Gao²², Woon-Puay Koh²³, Yong-Bing Xiang²², Ze-Zhong Tang²⁰, Jin-Hu Fan²¹, Jing-Jing Han^{5,18}, Sheng-Li Zhou⁵, Peng Zhang⁵, Dong-Yun Zhang⁵, Yuan Yuan⁵, Ying Huang¹, Chunling Liu¹, Kan Zhai¹, Yan Qiao¹, Guangfu Jin⁹, Chuanhai Guo¹⁰, Jianhua Fu^{11,12}, Xiaoping Miao²⁴, Changdong Lu¹⁷, Haijun Yang¹⁷, Chaoyu Wang², William A Wheeler²⁵, Mitchell Gail², Meredith Yeager^{2,3}, Jeff Yuenger^{2,3}, Er-Tao Guo⁵, Ai-Li Li^{5,26}, Wei Zhang⁵, Xue-Min Li²⁷, Liang-Dan Sun⁶, Bao-Gen Ma²⁸⁻³⁰, Yan Li⁵, Sa Tang⁵, Xiu-Qing Peng^{5,6}, Jing Liu⁵, Amy Hutchinson^{2,3}, Kevin Jacobs^{2,3}, Carol Giffen²⁵, Laurie Burdette^{2,3}, Joseph F Fraumeni Jr², Hongbing Shen⁹, Yang Ke¹⁰, Yixin Zeng^{11,12}, Tangchun Wu²⁴, Peter Kraft³¹, Charles C Chung^{2,3}, Margaret A Tucker², Zhi-Chao Hou⁵, Ya-Li Liu^{4,5}, Yan-Long Hu^{4,5}, Yu Liu⁹, Li Wang^{4,32}, Guo Yuan^{4,5}, Li-Sha Chen^{4,5}, Xiao Liu⁹, Teng Ma⁵, Hui Meng⁵, Li Sun⁵, Xin-Min Li⁵, Xiu-Min Li⁴, Jian-Wei Ku^{5,33}, Ying-Fa Zhou^{5,31}, Liu-Qin Yang³⁴, Zhou Wang³⁵, Yin Li³⁶, Qiren Wang³⁷, Wen-Jun Yang³⁸, Guang-Yan Lei³⁹, Long-Qi Chen⁴⁰, En-Min Li^{41,42}, Ling Yuan³⁶, Wen-Bin Yue^{5,43}, Ran Wang⁵, Lu-Wen Wang⁵, Xue-Ping Fan⁵, Fang-Heng Zhu³⁴, Wei-Xing Zhao⁴, Yi-Min Mao⁶, Mei Zhang⁵, Guo-Lan Xing⁵, Ji-Lin Li⁴⁴, Min Han⁴⁵, Jing-Li Ren³², Bin Liu⁴⁶, Shu-Wei Ren⁴⁷, Qing-Peng Kong⁴⁸, Feng Li⁴⁹, Ilyar Sheyhidin^{50,51}, Wu Wei^{52,53}, Yan-Rui Zhang²⁸⁻³⁰, Chang-Wei Feng³², Jin Wang⁵, Yu-Hua Yang⁵⁴, Hong-Zhang Hao⁵⁵, Qi-De Bao⁵⁵, Bao-Chi Liu⁵⁶, Ai-Qun Wu⁵⁷, Dong Xie⁵⁸, Wan-Cai Yang⁴, Liang Wang^{4,59}, Xiao-Hang Zhao⁶⁰, Shu-Qing Chen⁶¹, Jun-Yan Hong^{61,62}, Xue-Jun Zhang⁸, Neal D Freedman², Alisa M Goldstein², Dongxin Lin¹, Philip R Taylor², Li-Dong Wang^{4,5} & Stephen J Chanock²

nature
genetics

Corrigendum: Genome-wide association study of esophageal squamous cell carcinoma in Chinese subjects identifies susceptibility loci at *PLCE1* and *C20orf54*



Worldwide Ranks of Cancer Mortality



DCEG Studies in China: Upper Gastrointestinal Cancers

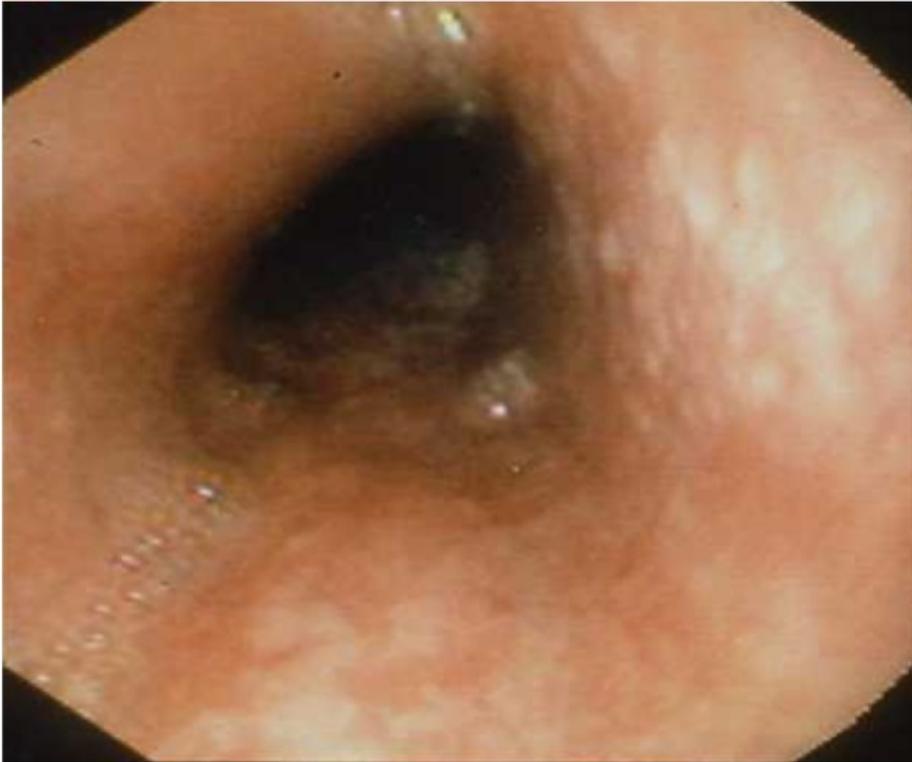
- **Nutrition Intervention Trials in Linxian, Henan**
 - Early detection of esophageal cancer
- ***H. pylori* treatment trial in Linqu, Shandong**
- **Genome-wide association studies**
- **Tooth loss & oral hygiene → microbiome**
 - Yunnan Tin Miner's Cohort with serial sputum samples



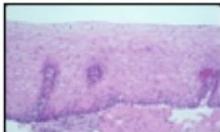
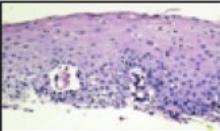
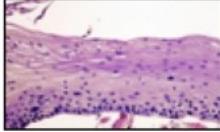
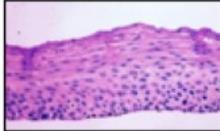
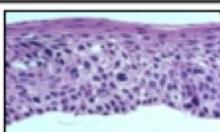
General Population NIT: Summary of Significant Trial Results

- **Selenium, β -carotene, and vitamin E**
 - Total mortality reduced 9%
 - Total cancer mortality reduced 13%
 - Total gastric cancer mortality reduced 21%
- **32,912 subjects being followed**
 - 6,332 incident UGI cancer cases
 - Observational studies
 - >100 publications
 - Serum selenium and UGI cancer risk
 - HPV and esophageal cancer risk

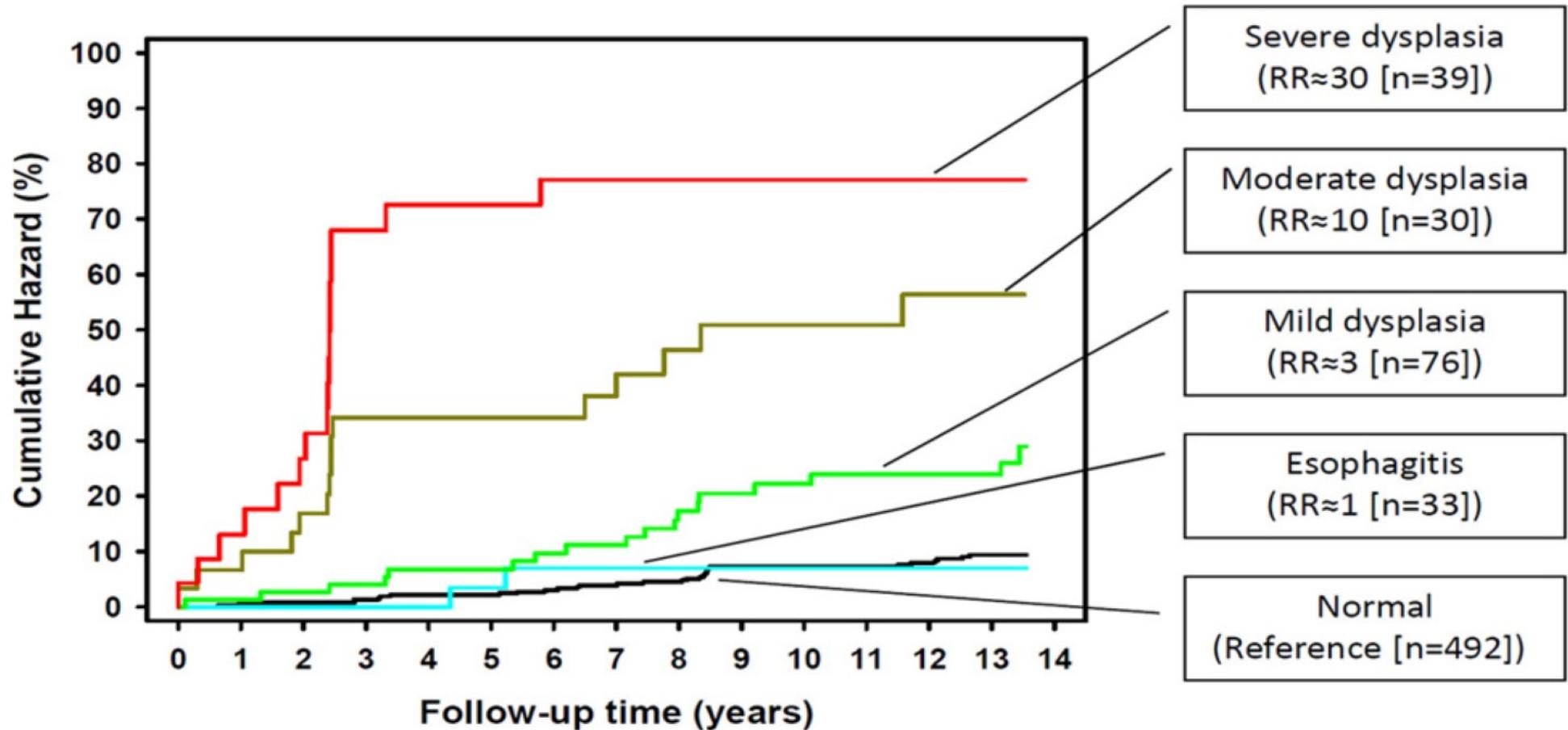
Early Detection and Intervention



Endoscopic Localization with Lugol's

Diagnosis		Sensitivity of Unstained Lesions
Normal		---
Esophagitis		---
Mild Dysplasia		63%
Moderate Dysplasia		93%
Severe Dysplasia		96%

Squamous Dysplasia is the Precursor



Components of Screening Program

Component	Complete
ID of precursor lesions	✓
Primary screen	✓
Endoscopic localization	✓
Staging	✓
Therapy	✓

Implementation of the Screening Program

VOLUME 33 · NUMBER 17 · JUNE 10 2015

JOURNAL OF CLINICAL ONCOLOGY

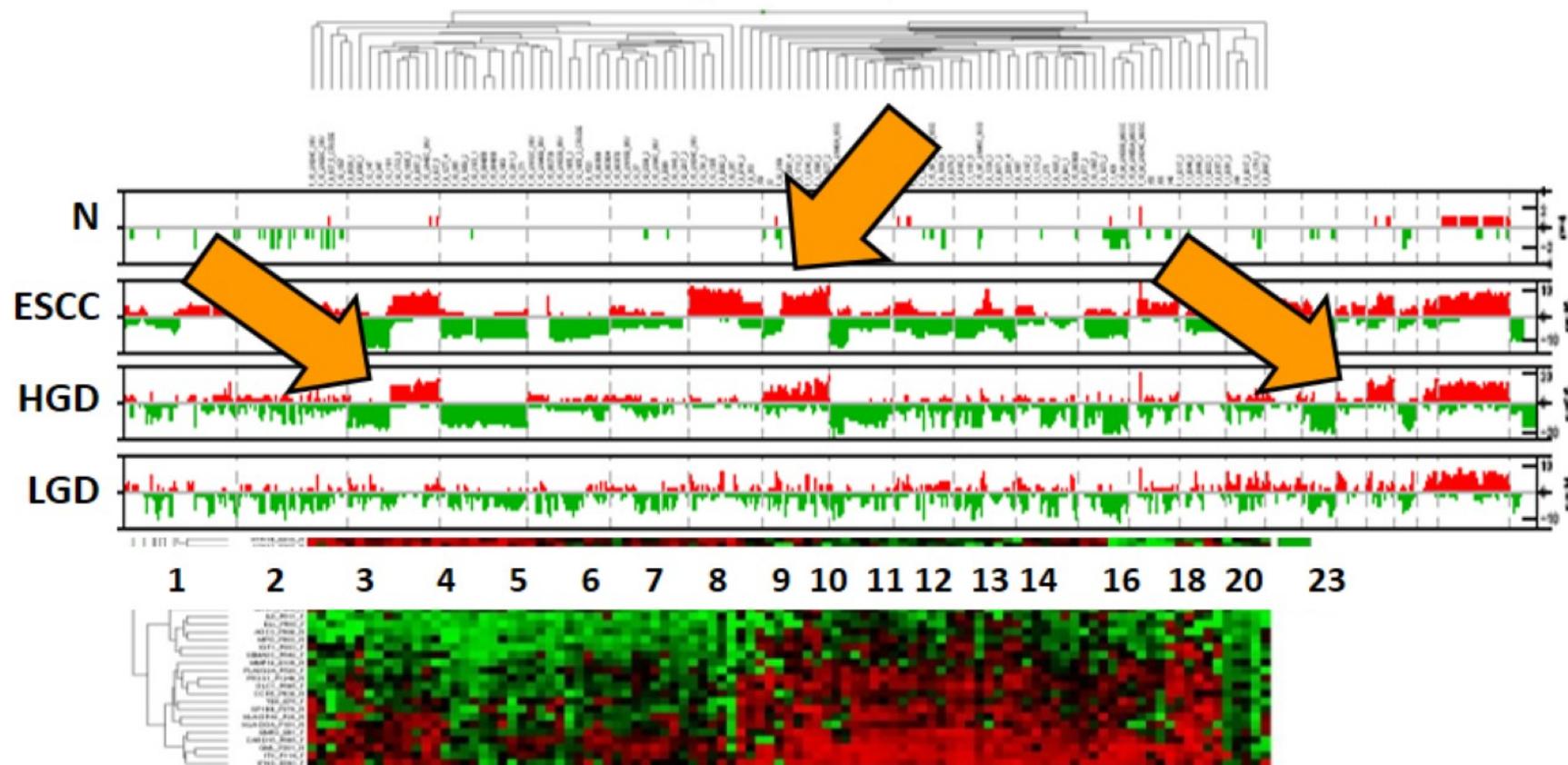
ORIGINAL REPORT

Long-Term Follow-Up of a Community Assignment, One-Time Endoscopic Screening Study of Esophageal Cancer in China

Wen-Qiang Wei, Zhi-Feng Chen, Yu-Tong He, Hao Feng, Jun Hou, Dong-Mei Lin, Xin-Qing Li, Cui-Lan Guo, Shao-Sen Li, Guo-Qing Wang, Zhi-Wei Dong, Christian C. Abnet, and You-Lin Qiao

- **34% reduction in ESCC mortality**

Improved Primary Screening



A

B

