Relation of colorectal cancer risk to faecal microbiome profile: why we need a prospective study

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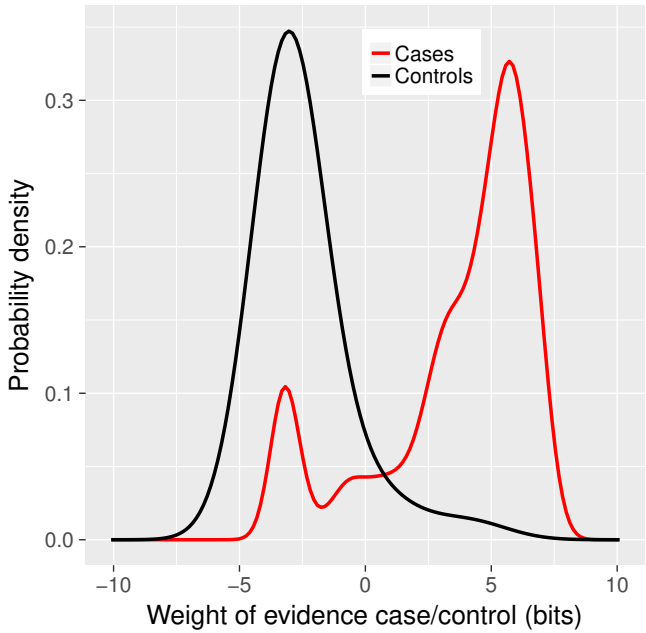
Limitations of bowel cancer screening with faecal immunochemical test (FIT) alone: reanalysis of Baxter et al. (2016)



At test threshold of 3 bits: 1 / 15 of those who test FIT-positive will have cancer, but only 61% of cancers will be screen-detected

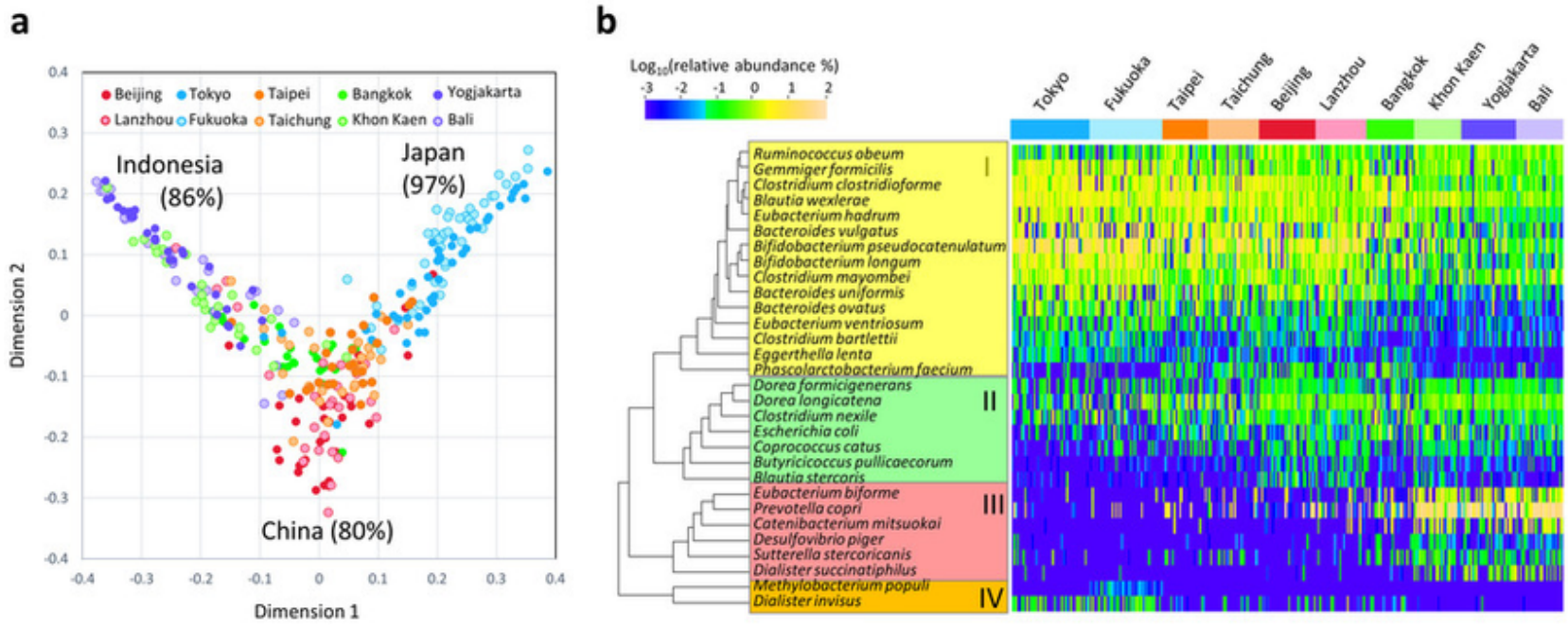
Towards a "learning health system"

- The Innovative Healthcare Delivery Programme seeks "to change fundamentally the way data and analytics are used to drive improvement in health outcomes"
  - Collaborative programme embedded in the Farr Institute Scotland (http://www.farrinstitute.org/partnerships/ihdp)
  - Joint Strategic Board chaired by the Director-General for Health and Social Care, includes NSS Chief Executive
- Initial focus is on the design, development and implementation of a cancer intelligence framework for Scotland
  - "building on recent developments and investments in informatics, data analytics, digital health, genomics and stratified medicine."

The bowel microbiome

- DNA sequencing has shown that the colonic microbiome consists of hundreds of "species" (taxonomic units)
  - microbiome profiles vary between individuals - many species are present in only a small proportion of individuals
  - Individual differences in microbiome profile are stable over at least five years
- Full profile by DNA sequencing is expensive
  - low-cost customized assays of $<$50 species are feasible
- Microbiome profile can be measured on leftover faecal material in FIT cartridges

Geographic variation in microbiome profile



Nakayama J *Scientific Reports* 2015: 8397

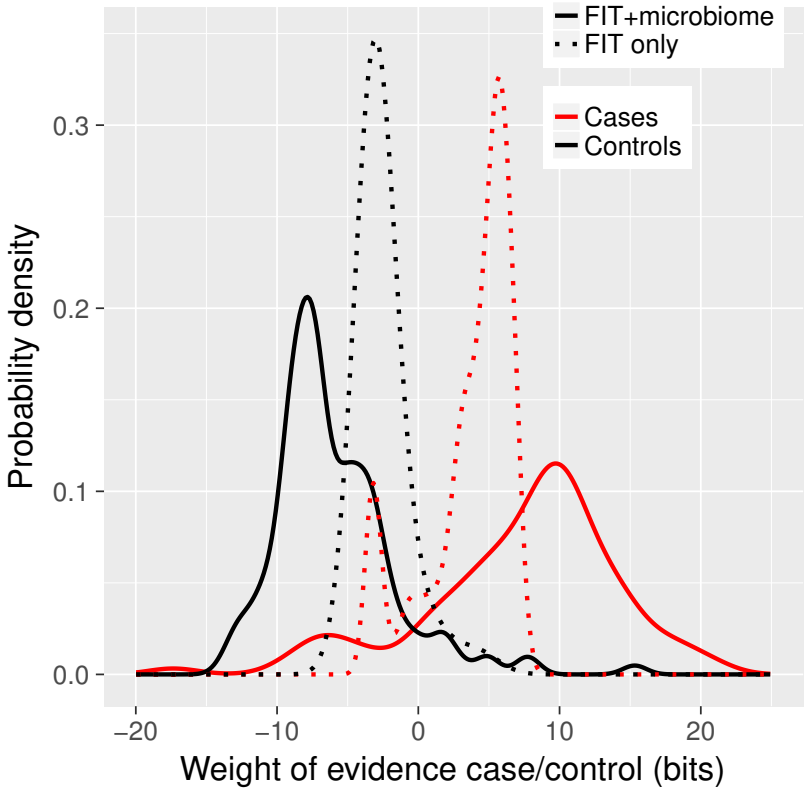
Can the bowel microbiome profile be changed?

- Diet: weight loss, non-starch polysaccharide
- Probiotics: mostly for *Lactobacillus* strains
- Antimicrobial therapy - disrupts microbiome
- Faecal transplant - effective treatment for recurrent *Clostridium difficile* infection

Relation of the colonic microbiome to colorectal cancer

- Experimental - altering microbiome alters cancer rates in mice
- Studies in humans - microbiome in biopsy samples and stool samples differs between people with and without colorectal cancer
    - All studies far have been in symptomatic people referred for colonoscopy

Adding microbiome profile to FIT doubles the predictive information (reanalysis of Baxter et al 2016)



Adding microbiome profile to FIT increases information for discrimination from 3.0 to 6.4 bits

Why a prospective study of relation of microbiome profile to colorectal cancer in asymptomatic individuals is needed

- A prospective study is required to establish
  1. whether the microbiome profile can detect cancers missed by FIT screening
  2. whether the relationsip between microbiome profile and cancer is causal.
- This prospective study has to be very large
- to accumulate 100 interval cancers over two years requires at least 120,000 consented samples linked to cancer follow-up.
  - very expensive as a standalone project
  - can be done at moderate cost by suspending it from the Bowel Screening Programme
- Unless a special case is made that consent is infeasible, consent is required for DNA analysis (Human Tissue Act) and for the Public Benefit and Privacy Panel to approve linkage to NHS data