What have we learned so far from the “Children of 1997”?

Gabriel M Leung
Hong Kong: recent history of rapid transition

Population mainly temporary young migrants looking for work  Baby boom

Cross-border marriage - mainly migrant mothers for family union

Living conditions in HK were better than in the neighboring provinces by 1930s

Anomalies in chronic disease - IHD

Why hasn’t an epidemic of ischemic heart disease (IHD) among men occurred in China with economic development?

Anomalies in chronic disease - Diabetes

- Low rates of IHD in China despite high rates of diabetes
- High rates of diabetes in China at low levels of obesity

Anomalies in chronic disease - COPD

Ranking of age-standardized years of life lost (YLL) rates in 2010 (1 representing country with the lowest YLL)

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<tr>
<th>Men</th>
<th>Stroke</th>
<th>Ischaemic heart disease</th>
<th>Road injury</th>
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- High rates of chronic obstructive pulmonary disease (COPD) in China

“If the observed trends continue, developed countries will continue to face an obese population a high prevalence of diabetes mellitus and hypercholesterolemia, whereas developing countries will be confronted by a combination of obesity, hypertension and diabetes mellitus. The diseases of affluence paradigm seems inadequate for explaining the nuances in the global epidemiology of cardiovascular risk factors and should be replaced with a more refined framework that better informs policy and intervention.”
Childhood adiposity epidemic in Hong Kong

Upward trend of childhood adiposity has concomitantly occurred with economic development over the past 50 years, with a clear shift of the entire BMI distribution.


Divergent trends of childhood blood pressure

Secular trend of childhood BP in Hong Kong remains unknown; downward BP trend in US persists despite increasing overweight trend while upward BP and overweight trends concur in China


Declining trends of pubertal timing

Early puberty is associated with IHD and hormone-related cancer with average age at puberty has decreased sharply with economic development. Girls with earlier menarche also have twice the risk of developing asthma than those with later menarche.


Declining trends of infectious disease burden

Infant mortality rate had significantly declined since 1950s in Hong Kong. Infection-related mortality for Infants and children under 5 maintains at very low rate.
Life course approach

Exposures at critical window or accumulating across different life course contribute to natural history of disease

A = normal development and decline;
B = exposure in early life reducing functional capacity;
C = exposure acting in mid to later accelerating age-related decline

Some factors which result in low birth weight might also cause diabetes, but seem unlikely that these same factors also cause ischemic heart disease

What about the role of overall growth patterns and early life exposures on health?

Potential determinants of childhood health

- Secondhand smoking
- Breastfeeding
- Timing of solid food introduction
- Child care
- Dairy product
- Mode of delivery
- Birth weight
- Gestational age
- Birth order
- Unknown biological factors
- Growth hormone
- Sex steroids
- Growth patterns at different phases
“Imprint of time”

1. Supreme difficulty of reversing disparities in health within a short time frame suggests a role for cohort/inter-generational effects

2. Cohort effects are increasingly recognized

3. Epigenetics provides a mechanism

Genetically identical

different maternal diet
Check consistency in different settings

Problems:
• Many epidemiologic findings are a reflection of confounding
• Some well-accepted dogmas are myths
• Implementing public health policy based on myths may be harmful

Solutions:
• Check the associations in a ‘negative control’ setting i.e., with different confounding structure
• Do an RCT
Uniqueness of Hong Kong’s “Children of 1997”

First post-colonial generation
- Chinese identity mixed with a western heritage
- First Chinese “first-world” generation
- Growing up in a resource-rich Chinese environment

Last Hong Kong generation with grandparents mainly born and brought up in pre-industrial China

Only large active Chinese birth cohort, with many differences from more commonly studied western populations
- Diet and lifestyle
- Child care, child rearing
- Less socio-economic patterning of BMI

Provides local evidence
8,327 infants born in Hong Kong in April and May 1997

**Overview of Hong Kong’s “Children of 1997”**

**Active follow-up**
- Infant health and lifestyle survey

**Passive follow-up**
- Survey I, Survey II, Survey III

**Body Mass Index**
\[ \text{BMI} = \frac{\text{weight}}{\text{height}^2} (\text{kg/m}^2) \]
- Weight and height: record linkage with Maternal and Child Health Centres, Student Health Service

1. Sex and age specific BMI *z-score* relative to WHO growth standard
2. *Overweight/obesity*: international obesity task force (IOTF)

**Public hospital use**

Physical and psychological assessments from the Student Health Service

Deaths from the Department of Health
“Infant lifestyle and health survey”

Originated by
• Professor TH Lam (HKU) with Department of Health

Research question
• The effect of secondhand smoking and breastfeeding on infant health

Design
• Recruited from all government well-baby clinics
• Carer completed questionnaires at 0, 3, 9 and 18 months

Participants
• All infants born in Hong Kong in April and May 1997 (88% of index births)
Revive “Infant lifestyle and health survey”

Resurrected and conceived by
• Professor Gabriel Leung and Dr Mary Schooling
  with Department of Health

1) Record linkage (2004-06)

2) Re-establish contact (2007-08)
• Letters
• Newsletters
• Cards, gifts
• Phone calls
• Press release
• Website

3) Postal and telephone surveys (2008-12)
• Family history and lifestyle (2008-10)
• Psychological well-being (2010-12)
• Waist and hip circumference (2012)

4) In-person follow-up (2010 to present)
• Pilot 1 of 40 in 2010
• Pilot 2 of 225 in 2011
• Pilot 3 of 502 in 2012
• Create Biobank in 2013
Approach to research

- Confirm or refute empirically driven hypotheses in a ‘negative control’ setting
- Use methods more suited to establishing causality
- Follow a coherent research program
Widely published findings

- Important information concerning the local health effects of secondhand smoking

- Contributed to the ban on smoking in all indoor public places subsequently implemented in Hong Kong
Important information concerning the local health effects of breastfeeding

Widely published findings

- Contributed to the change in the Hospital Authority’s infant formula procurement policy in Hong Kong
Positive findings on childhood overweight

Potential explanations (Informal child care):
1. Parents may be more likely to adhere to child rearing recommendation
2. Grandparents or domestic helpers may be less physical active and less likely to restrict child’s access to energy-dense favorite foods and television viewing

Potential explanation (Paternal smoking):
1. Adverse effect of secondhand smoke on child cognition and social behavior implies its possibility on appetite or metabolic control
Null findings on childhood overweight

Cesarean birth

“+” in most Western studies

“Null” in our cohort

Key confounders in Western population
- Low socioeconomic position (SEP)
- Maternal overweight
- Maternal smoking

Less influential factors in our Chinese cohort
- Not always associated with low SEP
- Maternal overweight – less prevalent
- Maternal smoking – uncommon

Childhood obesity

Never breastfeeding

Early solid food introduction

Low dairy product intake
Findings on adolescent blood pressure

Breastfeeding was unrelated to adolescent blood pressure in our cohort, perhaps because high SEP is key confounder in Western population but is not associated with sustained breastfeeding in our Chinese cohort.

Birth weight and infant growth had limited impacts on adolescent blood pressure, which was more strongly related to recent growth and current size.
Findings on pubertal timing

Breastfeeding and childhood dairy product intake was not associated with pubertal timing

Early infection was associated with later puberty, suggesting that less infection with economic development could contribute to earlier puberty

Faster childhood height growth was associated with earlier puberty, but not birth weight

Premature births was associated with later puberty
More findings from “Children of 1997”

- Rapid infant growth
  - Weight
  - Age
  - "Null"
- Lower pubertal muscle mass
- Rapid infant growth
  - Weight
  - Age
  - "Null"
- Breastfeeding
  - "Not clear"

- Higher childhood BMI
  - "+
- Higher blood glucose
  - "+
- Infection
- Mental health
  - "Not clear"
Public health implications

• Short-term effects of second-hand smoke and breastfeeding

• Long-term effects of second-hand smoke
  More infections into childhood
  Obesity in childhood

• Little long-term effect of breastfeeding on obesity, infections, blood pressure, timing of puberty or mental health

• Little effect of Cesarean section, timing of solid food introduction or use of dairy products on obesity

• Childhood BMI has changed dramatically in the last 50 years. Modifiable factors driving early BMI, such as informal child care or paternal smoking are important, but unlikely to explain all the change
Etiological implications

- Little effect of birth weight on blood pressure or timing of puberty
- Early infections and premature birth associated with later puberty
- Lack of muscle mass at puberty may be a key driver of diabetes
- Unclear role of rapid infant weight growth
  No reduction in infectious illness
  Higher BMI
- Faster height growth is associated with earlier puberty
Strengths and limitations

Strengths

• Large sample
• Detailed information on growth and BMI
• Unique setting, enables us to test empirically derived hypotheses from the west
• Provides useful etiological information

Limitations

• Exposures not always well defined
• Associations may be different at the completion of growth
• Cannot identify body composition from BMI
Future directions

Epigenetics
  • Are there epigenetic effects on growth axes and do they affect health?

Genetics
  • GWAS
  • Mendelian randomization

Microbiome
  • Effects on obesity and metabolism
  • Trade-offs of chronic infections
  • As an endocrine organ
Publications

**Infant Health and Lifestyle Survey**


**Children of 1997**

The team

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Dr SL Au Yeung
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Rita Hou
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Pediatrics
Professor EAS Nelson
Professor AM Li
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Dr P Ip

IHP
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Dr D McFarlane
Dr A McManus

Nursing
Dr M Tarrant
Discussion Session

For further information,

COHORT PROFILE

Cohort Profile: ‘Children of 1997’: a Hong Kong Chinese birth cohort

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