

The power of cohort studies in population health

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Where is the power of cohort studies?



Temporality and potentially causality

Multiple outcomes

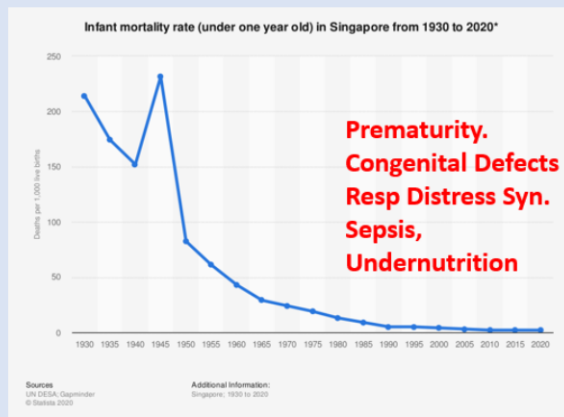
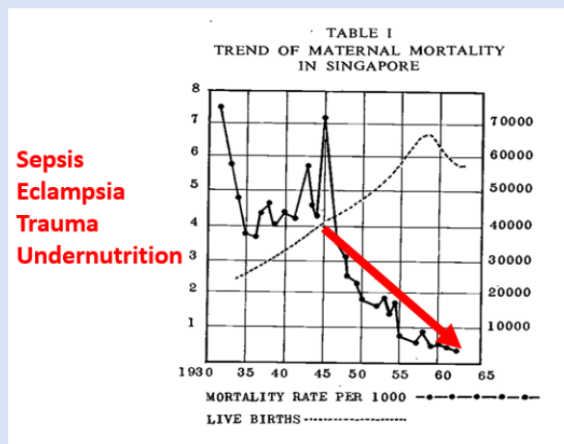
Reflect real-world conditions

Longitudinal data

Minimized recall bias

Health issues - and the world - have changed rather rapidly

Dramatic reduction in **Maternal Mortality** (2.5/100,000) and **Infant Mortality** (2/1000)



21st Century Challenges in MCH

MMF Triad of Health Issues

Metabolic Disorders

NPHS National Population Health Survey 2022

| | | | |
|-----------------|-------------------|-------------------|---------------------|
| DM 9% | HLD 32% | HTN 37% | Ow/Ob 59% |
|-----------------|-------------------|-------------------|---------------------|

BMI ≥23

Maternal-child Ow/Ob



Poor Mental Health

NPHS National Population Health Survey 2023

| | | | |
|-----------------------|-----------------------|----------------------|----------------------|
| 26% 18-29 y | 17% 30-39 y | 13% 40-49y | 11% 50-59y |
|-----------------------|-----------------------|----------------------|----------------------|

General Health Questionnaire (GHQ-12)

Maternal depressive symptoms



Ultra-Low Fertility

TFR Total Fertility Rate of Singapore's Residents

| | | |
|---------------------|---------------------|---------------------|
| 1.83 1990 | 1.26 2005 | 0.97 2024 |
|---------------------|---------------------|---------------------|



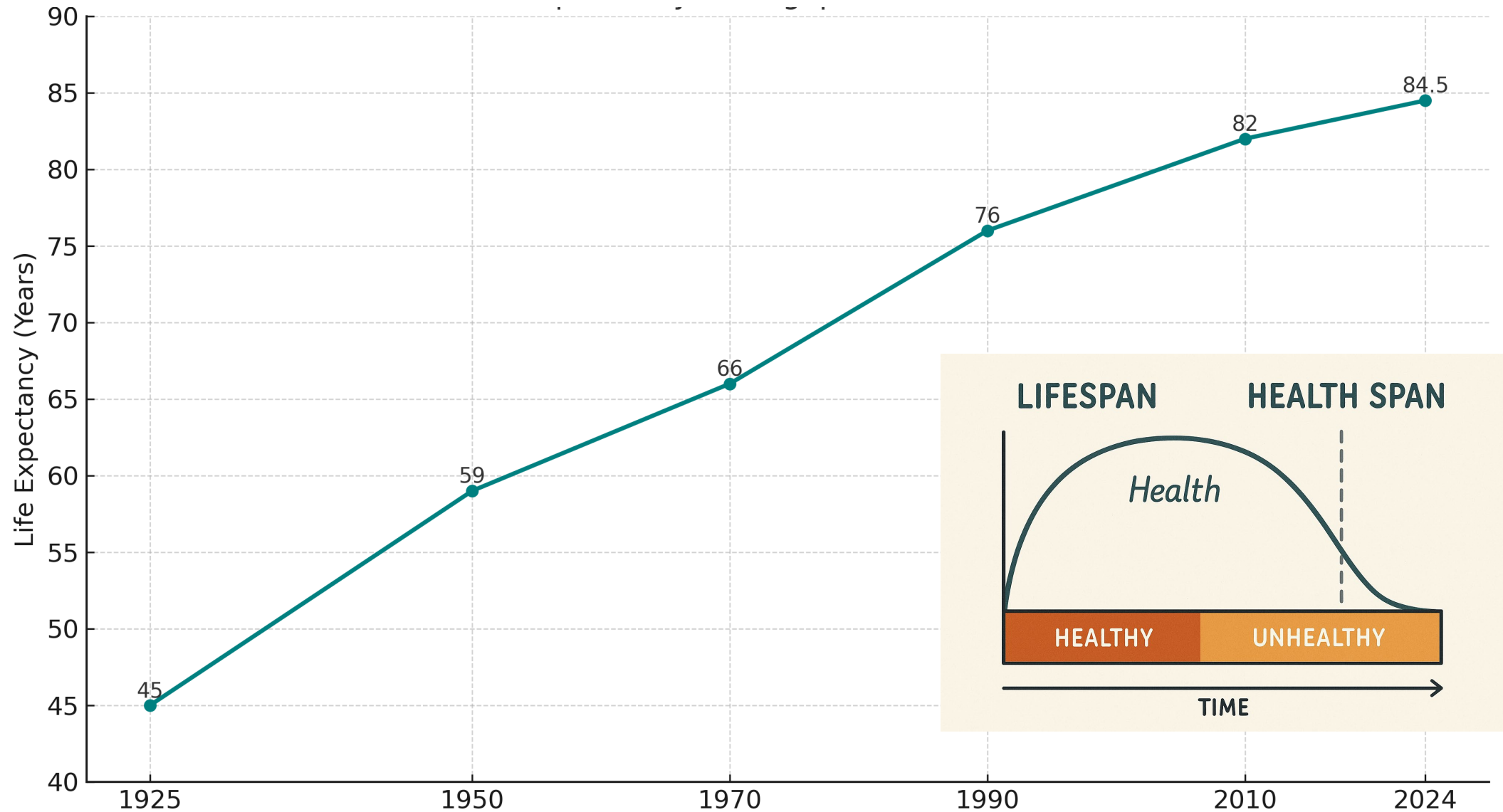
Women trying to conceive over 1 yr



Loo et al., Eur J Epidemiol. 2020; Kee et al., Arch Womens Ment Health. 2021; MOH Singapore, 2021; NPHS 2022 & 2023 Report, MOH Singapore; Singapore Department of Statistics, 2025

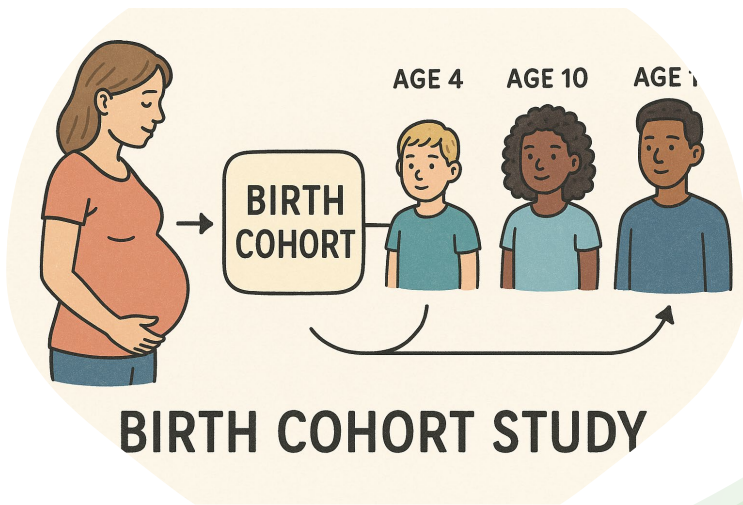
Restricted, Sensitive (Normal)

Life expectancy in Singapore over 100 years



GUSTO

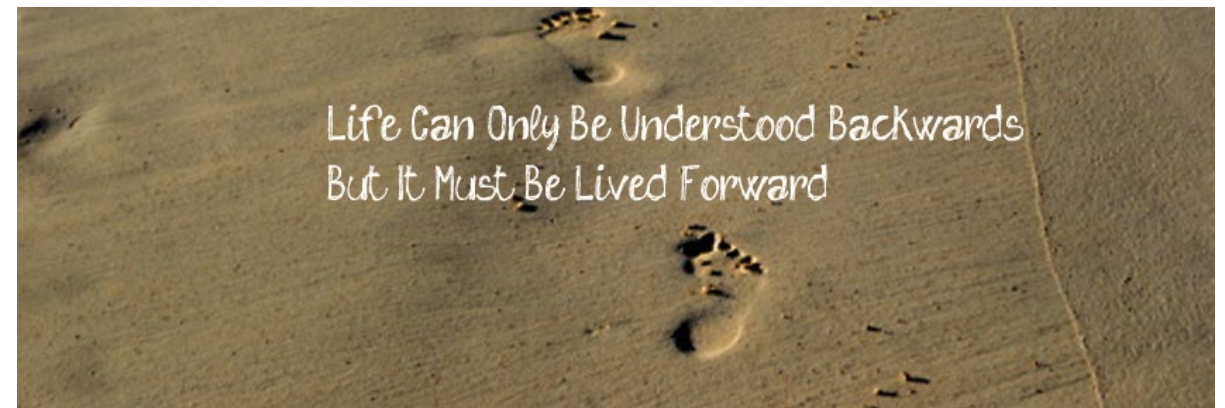
A birth cohort study



- The **Growing Up in Singapore Towards healthy Outcomes (GUSTO)** study was established in 2009 to investigate how early life factors influence the development of metabolic and neuro-developmental conditions.
- Recognizing a significant increase in non-communicable diseases - like diabetes in Asia - researchers aimed to understand the early life determinants contributing to this trend.

Why are longitudinal cohort studies important ?

Longitudinal cohort studies can offer insights across a lifespan



“At first sight it may seem improbable that events occurring in existence could produce changes 50-70 years later”

Hales & Barker, 1992, Diabetologia



1st Window

The **first 1000 days** of life is widely recognised as a critical development period for the body, brain and immune system.



Why Your DNA Isn't Your Destiny | Jan. 18, 2010
Cover Credit: PHOTOGRAPH FOR TIME BY KEVIN VAN AELST



How the First Nine Months Shape the Rest of Your Life | Oct. 4, 2010
Cover Credit: MERRICK MORTON / COLUMBIA

2nd Window

The adolescent period (10-24 years) has been identified as a **crucial second window** of development for body, brain and social and psychological changes





- Launched in 2009
- 1247 mother-child pairs
- 3 Asian ethnic groups
- Very close longitudinal follow-up
- Very deep phenotyping & biosampling
- >15,000 phenotypes collected across 10 domains



IN UTERO



BIRTH

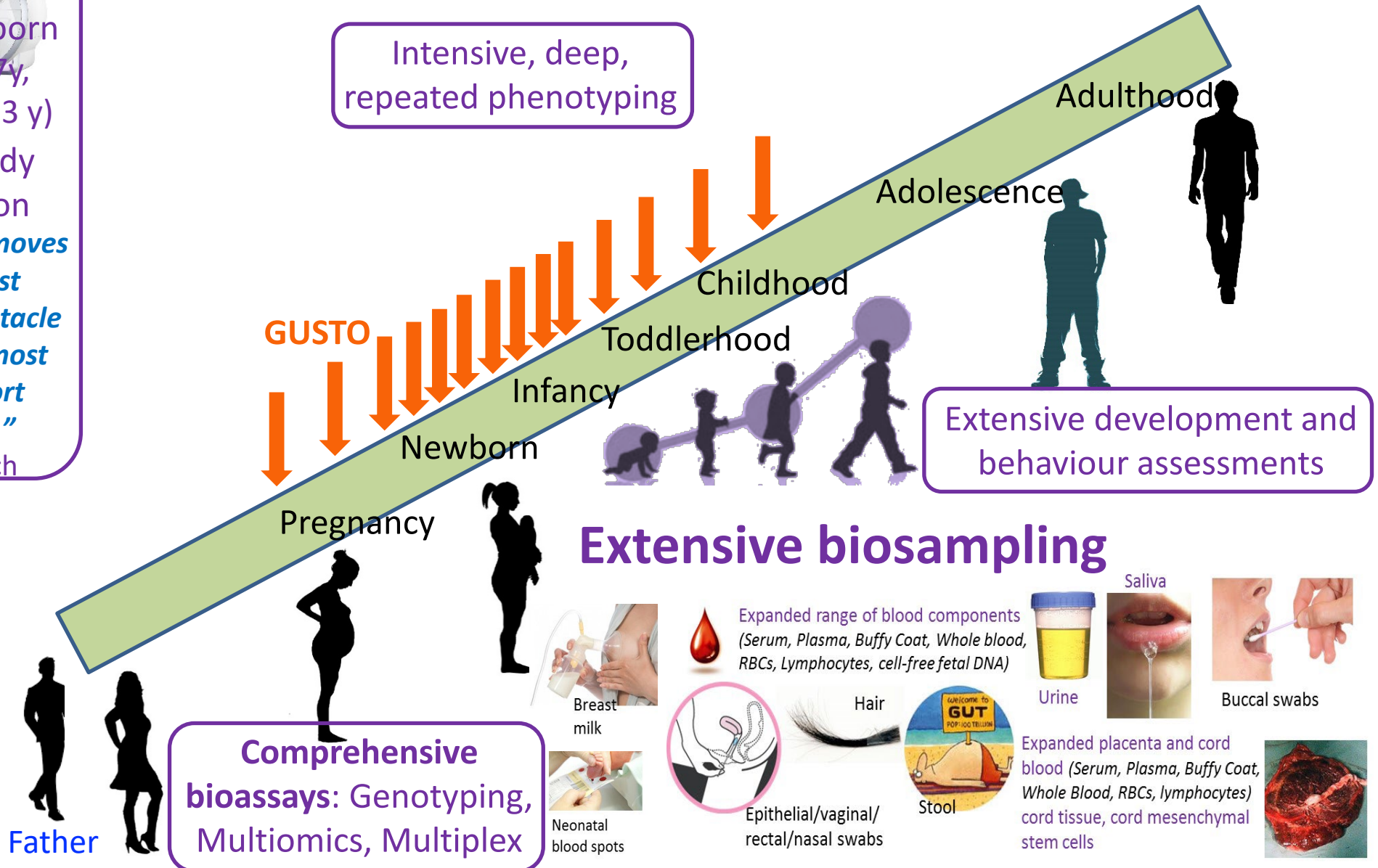


INFANCY & CHILDHOOD



Unique developmental cohort

MRI of newborn
(4.5y, 6y, 7y,
10.5 y & 13 y)
Brain & Body
composition
“(GUSTO) removes
the biggest
scientific obstacle
that faces most
birth cohort
studies...”
Am.J.Psych





Some Research Highlights & Key Insights

Transforming Maternal Metabolic Health in Singapore

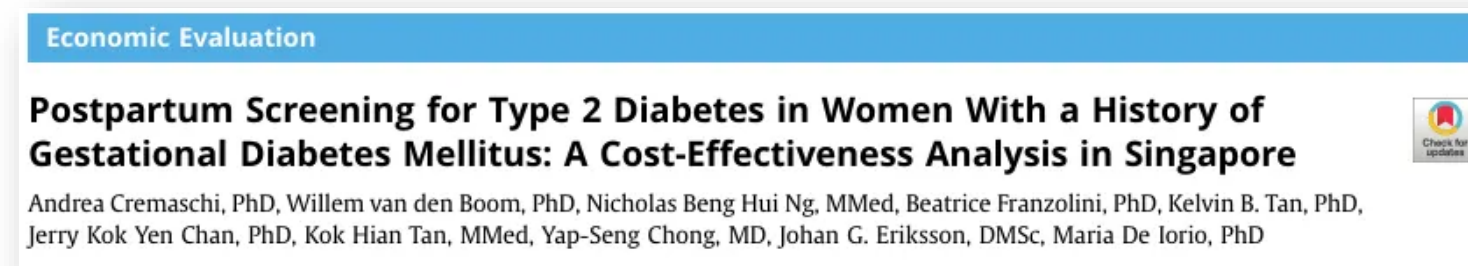
GUSTO's research on gestational diabetes (GDM) led to policy changes and long-term benefits

2014



- **GUSTO: 1 in 5 women** affected by GDM
- **Half were missed** by prevailing (high-risk) screening
- Post-pregnancy, those with GDM are at **12x higher risk of diabetes**

2024



2016



Universal screening for GDM is **cost-effective** for reducing complications, compared to targeted or no screening

2018



National guidelines updated: **universal screening introduced**

Universal annual screening reduces costs by **\$19.4M** and adds **3.8 thousand QALYs** per cohort of pregnant women

Advancing Diabetes Risk Prediction: Machine Learning

JMIR DIABETES

Kumar et al

[Original Paper](#)

Machine Learning–Derived Prenatal Predictive Risk Model to Guide Intervention and Prevent the Progression of Gestational Diabetes Mellitus to Type 2 Diabetes: Prediction Model Development Study

Mukresh Kumar^{1,2,3}, BEng (Hons I); Li Ting Ang^{1,2}, BSc; Cindy Ho^{1,2}, BSc; Shu E Soh⁴, PhD; Kok Hian Tan^{5,6}, MBBS, MMed, MBA; Jerry Kok Yen Chan^{7,8,9}, MB BCh BAo (Hons), PhD; Keith M Godfrey^{10,11}, BMMed (Hons), PhD; Shiao-Yng Chan^{1,7}, MBBS, PhD; Yap Seng Chong^{1,7}, MBBS, MMed, MD; Johan G Eriksson^{1,7,12,13*}, MD, DMSc; Mengling Feng^{3,14*}, PhD; Neerja Karnani^{1,2,15*}, PhD

Machine Learning Models used to

- Predict which women with GDM are at risk of Type 2 Diabetes
- Predict preterm birth risk with high accuracy
- Identify non-invasive predictors of GDM – outperformed UK guidelines in assessing risk in Asians



ELSEVIER

Contents lists available at [ScienceDirect](#)

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice



Population-centric risk prediction modeling for gestational diabetes mellitus: A machine learning approach

Mukresh Kumar^{a,b,c}, Li Chen^a, Karen Tan^a, Li Ting Ang^{a,b}, Cindy Ho^{a,b}, Gerard Wong^a, Shu E Soh^d, Kok Hian Tan^{e,f}, Jerry Kok Yen Chan^{g,h,i}, Keith M Godfrey^j, Shiao-ying Chan^{a,g}, Mary Foong Fong Chong^{a,c}, John E Connolly^k, Yap Seng Chong^{a,g}, Johan G Eriksson^{a,g,l,m,1}, Mengling Feng^{c,*,1}, Neerja Karnani^{a,b,n,*,1}



International Journal of
*Environmental Research
and Public Health*



Article

Automated Machine Learning (AutoML)-Derived Preconception Predictive Risk Model to Guide Early Intervention for Gestational Diabetes Mellitus

Mukresh Kumar^{1,2,3}, Li Ting Ang^{1,2}, Hang Png^{1,2}, Maisie Ng^{1,2}, Karen Tan¹, See Ling Loy^{4,5}, Kok Hian Tan^{4,6}, Jerry Kok Yen Chan^{4,5,7,8}, Keith M. Godfrey⁹, Shiao-ying Chan^{1,8}, Yap Seng Chong^{1,8}, Johan G. Eriksson^{1,8,10,11,†}, Mengling Feng^{3,12,*,†} and Neerja Karnani^{1,2,13,*,†}

Mobile Health Interventions for Diabetes Prevention

HAPPY - **H**arnessing human **P**otential and improving health **sP**an in women and their children **studY**

GUSTO:

- GDM patients are at 12-fold higher risk of diabetes in the 4 – 6 years post-pregnancy
- Particularly those obese or overweight, or retained weight after delivery



- A novel, holistic digital intervention integrating mental health, diet and lifestyle
- Completed recruitment in Sep '24
- Data collection under way

scientific reports

OPEN

Combined analysis of gestational diabetes and maternal weight status from pre-pregnancy through post-delivery in future development of type 2 diabetes

Ling-Wei Chen^{1,3}, Shu E Soh¹, Kok Hian Tan^{5,7}, Yung Seng L¹, Peter D. Gluckman^{4,10}, Johan

Study on diabetes risk in mums to look at sleep, mental well-being

Lee Li Ying
Correspondent

A new four-year study aims to help women who have had diabetes while pregnant cut their risk of developing Type 2 diabetes later in life, by studying health factors such as mental well-being and

there are many reasons women who have gestational diabetes have a higher risk of Type 2 diabetes. One is increased weight gain during pregnancy, and another is that both disorders share a large number of genetic risk factors.

Lifestyle modifications like improving dietary intake and mental well-being and more physical activity can prevent or delay the on-

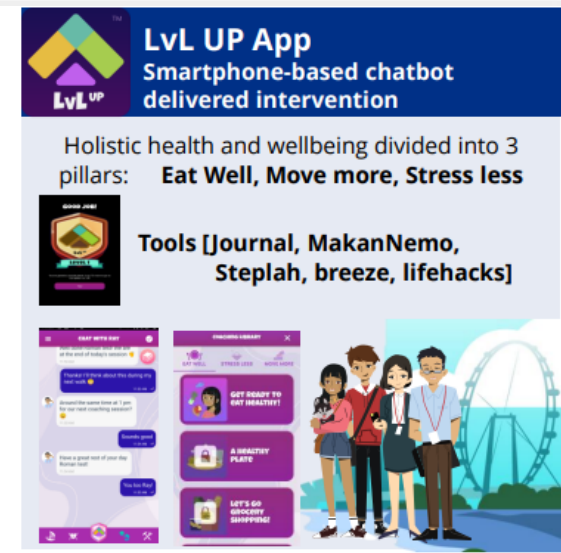
of developing Type 2 diabetes.

Study participants will wear a digital ring tracker to accurately measure their sleep or wake states for eight weeks.

The researchers are hoping to recruit 400 Chinese, Malay or Indian women between the ages of 21 and 45 who had gestational diabetes in the past decade, but have no current or past major health conditions, and are currently not expecting.

They will have to install the Happy app on their personal smartphones. "Happy" stands for "Harnessing human potential and improving health span" in women and their children study", which is the name of the study.

Developed by SICS, the Happy app will allow participants to track their health data such as



(SEC) SINGAPORE-ETH CENTRE



Maternal mental health & wellbeing

Improving Maternal Mental Health in Singapore

Practice-changing findings on maternal mental health and the impact on child development

2013- 2017

ARCHIVAL REPORT

Biological Psychiatry
A Journal of Psychiatric Neuroscience and Therapeutics

Prenatal Maternal Depression Associates with Microstructure of Right Amygdala in Neonates at Birth

Anne Rifkin-Graboi, Jordan Bai, Helen Chen, Waseem Bak'r Hameed, Lit Wee Sim, Mya Thway Tint, Birit Leutscher-Broekman, Yap-Seng Chong, Peter D. Gluckman, Marielle V. Fortier, Michael J. Meaney, and Anqi Qiu

RESEARCH ARTICLE

HUMAN BRAIN MAPPING

WILEY

Perinatal maternal depressive symptoms alter amygdala functional connectivity in girls

Ni Ni Soe¹ | Daniel J. Wen¹ | Joann S. Poh² | Yap-Seng Chong^{2,3} |
Birit Fp Broekman² | Helen Chen⁴ | Lynette P. Shek^{2,5,6} | Kok Hian Tan⁷ |
Peter D. Gluckman² | Marielle V. Fortier⁸ | Michael J. Meaney^{2,9,10} | Anqi Qiu^{1,2}

Correlation between a child's brain microstructure and in utero exposure to maternal depression & anxiety

2021
CHILD
Evidence
Brief

2015

White Paper to MOH



Maternal Emotional Well-being:

Screening and Management may benefit Singapore's future generations.

3 September 2015

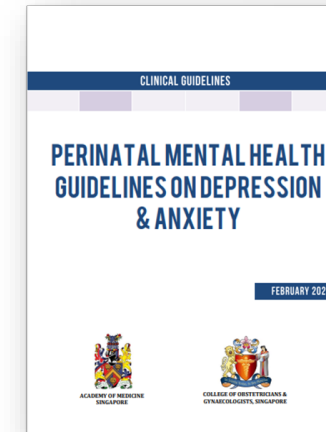
2023

THE STRAITS TIMES

New guidelines to support mental health of women during pregnancy and after birth



About 8% of expectant mothers found to have signs of prenatal depression following KKH screening



Singapore's **first clinical guidelines on perinatal mental health**, with KKH introducing **universal mental health screening**

Parenting intervention targeting emotion regulation

Bonding Before Birth (B3)



Findings from GUSTO, MAMS:

- Prenatal maternal depressive symptoms impact **child brain changes** associated with executive function and emotion regulation
- Maternal executive function, emotion and behavioural regulation **affect child executive function and emotion regulation**

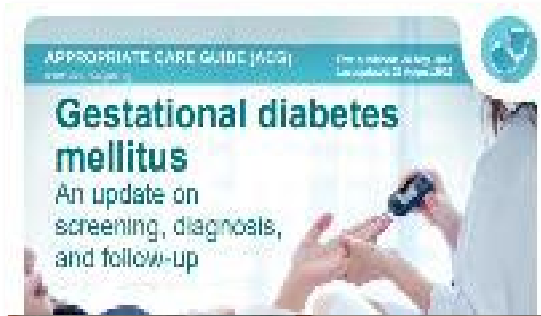
Bonding Before Birth Intervention

- Adaptive intervention **mobile health** trial in first-time expectant parents
- Mindfulness and cognitive-behavioural therapy-based
- Reinforcement learning, micro-randomisation in a cluster-randomised controlled trial

- Low cost, **scalable digital intervention** delivered during the antenatal period
- Involving **both parents**
- Emphasises **prenatal period as critical window for intervention**

Expected outcome: to **improve emotion regulation in parents** and children – promoting **child cognitive and socio-emotional development**

From evidence to impact



Gestational diabetes

- Recommendations for universal screening and follow-up



Maternal Mental Health

- Singapore's first Perinatal Mental Health Guidelines (College of O&G Singapore)
- Universal antenatal screening for mental health issues (KKH)



Childhood Activity

- Guidelines for 24-hour activity in children 0 – 6 years old (College of Paediatrics and Child Health)



Childhood Screen Time

- Guidance on Screen Use in Children: No screen time for children under 18 months of age (HPB and MOH)

How do contextualized, longitudinal studies like GUSTO benefit Singapore and Asia?

Provide detailed **descriptive and cumulative data** on a group of Singaporeans growing up *today*

In-situ look at how individual, social and environmental factors affects health across the current generation, and how the dynamic environment interacts with growth and well-being

Microscope

Findings represent **local ethnic & cultural norms**



Pathways

Identifies actionable pathways from evidence to implementation
GUSTO offers opportunities to map trajectories and understand not just **modifiable factors**, but relevant pathways for interventions

Path-finds serendipitous insights
Through repeated, **longitudinal measures** of development in association with environmental factors, for problems not previously envisaged

Pathfinder



Why were the cohorts set up in SG?

Limitations of other existing cohorts:

- 1) Most recruited only from birth onwards
- 2) Comprised predominantly White Caucasian
- 3) Narrow range of data, biosampling and clinical measures
- 4) Infrequent follow-up during greatest growth periods



Why Singapore?

- 1) Three major Asian ethnic groups: Chinese, Malay, Indian
- 2) Adequate Resources, Skills and Infrastructure
- 3) Literate women willing to participate in such research
- 4) Accessible population within small geographical space with limited migration



SINGAPORE

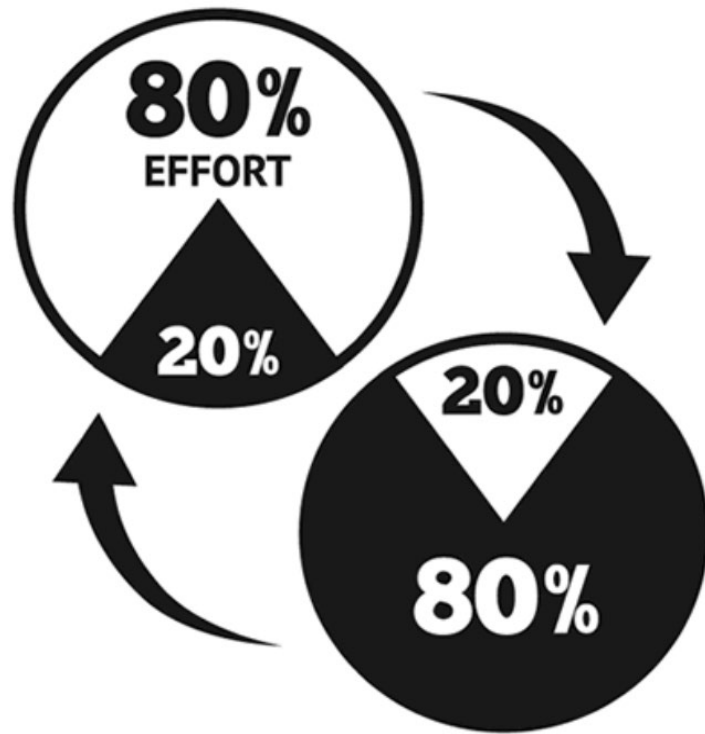


NEW ZEALAND



DENMARK

Pareto principle



nature
human behaviour

ARTICLES

<https://doi.org/10.1038/s41562-019-0810-4>

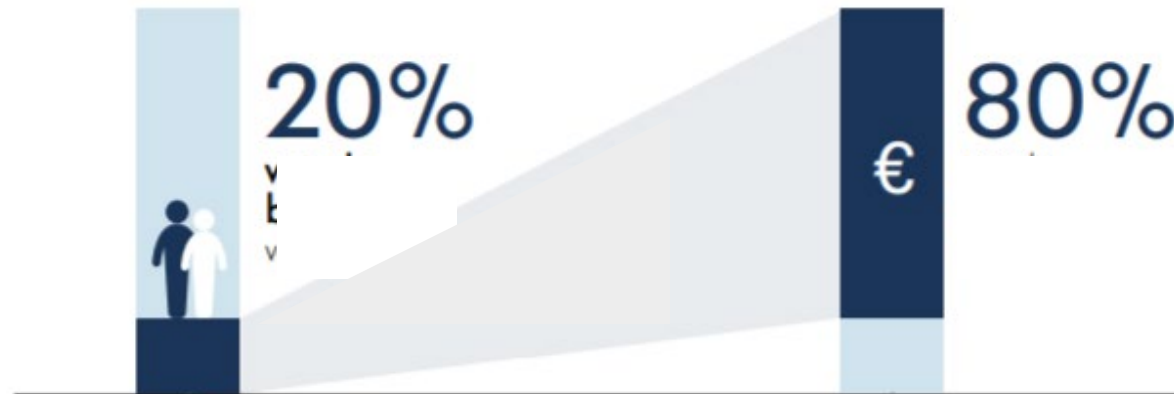
Clustering of health, crime and social-welfare inequality in 4 million citizens from two nations

Leah S. Richmond-Rakerd^{1,2*}, Stephanie D'Souza³, Signe Hald Andersen⁴, Sean Hogan⁵, Renate M. Houts¹, Richie Poulton⁵, Sandhya Ramrakha⁵, Avshalom Caspi^{1,6,7,8,9}, Barry J. Milne^{3,9} and Terrie E. Moffitt^{1,6,7,8,9}

Health and social scientists have documented the hospital revolving-door problem, the concentration of crime, and long-term welfare dependence. Have these distinct fields identified the same citizens? Using administrative databases linked to 1.7 million New Zealanders, we quantified and monetized inequality in distributions of health and social problems and tested whether they aggregate within individuals. Marked inequality was observed: Gini coefficients equalled 0.96 for criminal convictions, 0.91 for public-hospital nights, 0.86 for welfare benefits, 0.74 for prescription-drug fills and 0.54 for injury-insurance claims. Marked aggregation was uncovered: a small population segment accounted for a disproportionate share of use-events and costs across multiple sectors. These findings were replicated in 2.3 million Danes. We then integrated the New Zealand databases with the four-decade-long Dunedin Study. The high-need/high-cost population segment experienced early-life factors that reduce workforce readiness, including low education and poor mental health. In midlife they reported low life satisfaction. Investing in young people's education and training potential could reduce health and social inequalities and enhance population wellbeing.



Societal costs



Nearly all
had a non-
optimal start
in life



Longitudinal Cohort Studies Offer Insights Across a Life Span

The *Dunedin Multidisciplinary Health and Development Study*, New Zealand, is a birth cohort begun between 1972-3

It's original 1000+ participants are now >50 yrs old, with findings that have influenced policy practice in NZ and overseas

A world standard, the Dunedin Study has set the foundations and shaped our present understanding of how developmental origins have their place in influencing individual and community health & well-being

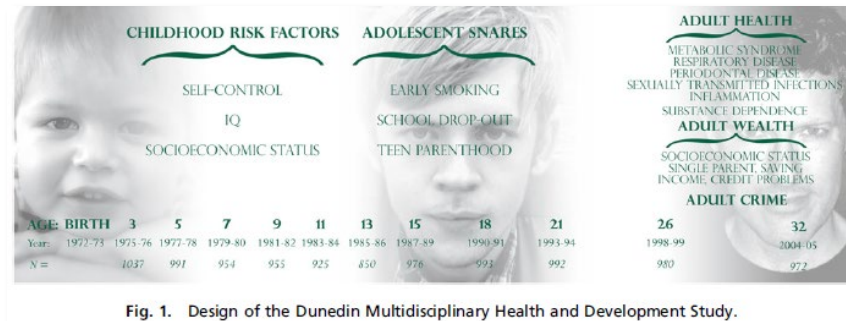


Fig. 1. Design of the Dunedin Multidisciplinary Health and Development Study.

Reaping the full value of longitudinal studies can take decades - but **adds significant value** to our understanding of human development and capital

Some highlights from the Dunedin Study

Childhood self-control promoted healthy ageing across various aspects of **physical, mental and social** wellness

Childhood self-control forecasts the pace of midlife aging and preparedness for old age

Leah S. Richmond-Rakerd^{a,1}, Avshalom Caspi^{b,c,d,e,f}, Antony Ambler^{a,g}, Tracy d'Arbeloff^h, Marieke de Bruine^b, Maxwell Elliott^b, HonaLee Harrington^b, Sean Hogan^g, Renate M. Houts^b, David Ireland^g, Ross Keenan^{i,j}, Annchen R. Knodt^b, Tracy R. Melzer^k, Sena Park^b, Richie Poulton^g, Sandhya Ramrakha^g, Line Jee Hartmann Rasmussen^{h,l}, Elizabeth Sack^b, Adam T. Schmidt^m, Maria L. Sison^b, Jasmin Wertz^b, Ahmad R. Hariri^b, and Terrie E. Moffitt^{b,c,d,e,f}

Just 20% of the study participants accounted for a disproportionately high economic & social burden



54%
Cigarettes
smoked



66%
Welfare
benefits



81%
Criminal
convictions

Published: 12 December 2016

Childhood forecasting of a small segment of the population with large economic burden

Avshalom Caspi, Renate M. Houts, Daniel W. Belsky, HonaLee Harrington, Sean Hogan, Sandhya Ramrakha, Richie Poulton & Terrie E. Moffitt

4 predictive factors for this high risk group:

- **Low SES in childhood**
- **Childhood maltreatment**
 - Low IQ
- **Low Self-Control**

Importance of a strong foundation



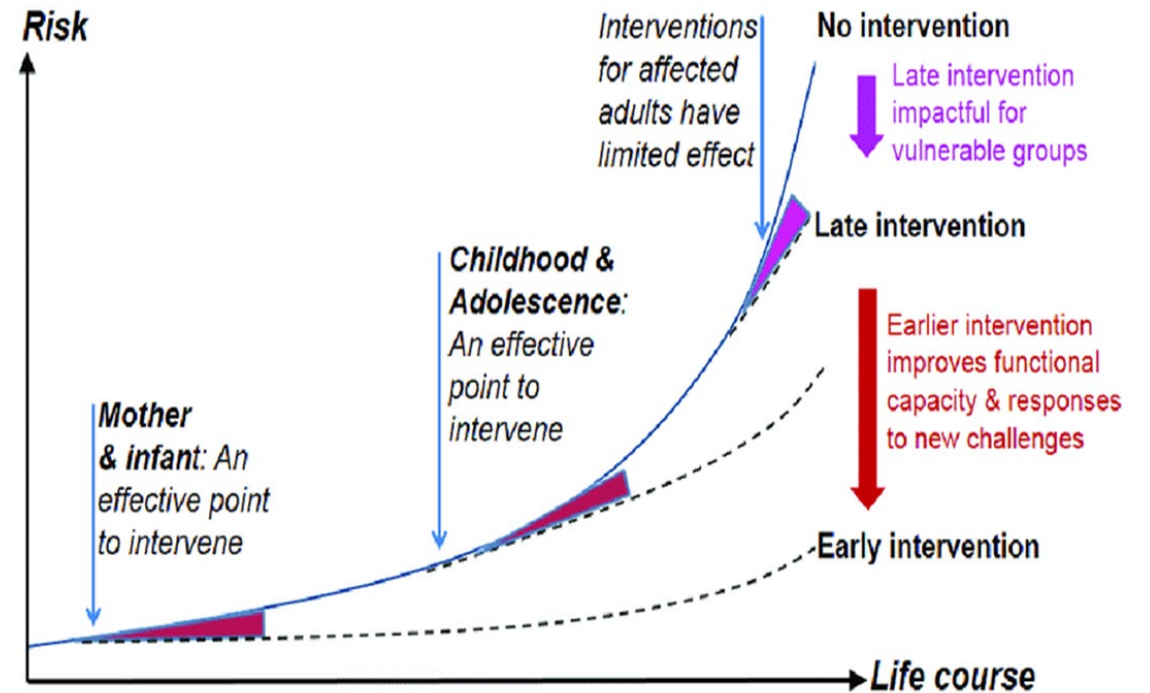
Building a solid foundation in the early years of a child's life will not only help him or her reach their full potential but will also result in better societies as a whole

Give Every Child the Best Start



"It is easier to build strong children than to repair broken adults."

- Frederick Douglass -





Thank you !!
GUSTO – participants,
staff and funders

