Light on the Longterm: from the British cohorts to the US National Children’s Study

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UCLA Center for Healthier Children Families & Communities

Friday, April 3rd 2009
Neville Butler Memorial Lecture
London
Child poverty in perspective:

An overview of child well-being in rich countries

A comprehensive assessment of the lives and well-being of children and adolescents in the economically advanced nations
<table>
<thead>
<tr>
<th>Country</th>
<th>Average rank</th>
<th>Material Situation</th>
<th>Health and Safety</th>
<th>Education</th>
<th>Children’s relationships</th>
<th>Subjective Well-being</th>
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UNICEF 2007
Child well-being by child poverty $r=0.75$

Bradshaw, 2007
Neville Butler

- A Children’s Doctor
- A Researcher
- A Translator
- An Inventor
- An Advocate
- An Investor-
- A Visionary
British Birth Cohort Studies have influenced

- Micro Level
  - Specific policies
  - Specific research questions

- Macro
  - Policy Strategies
  - Research Programs and Paradigms

- Meta-Historical
  - Epochal transformation in how we understand health, delivery of health and social services,
Presentation

- Historical Context- 3 Eras of Health
- Impact and Importance of the British Birth Cohort Studies
- Paradigm shift in Life Course Health Development
- US National Children's Study
- Transformation of Health and Health Care From 2.0 to 3.0
- The Emerging Future: What Health 3.0 will mean
Three Era’s of Health and Health Care

- 1st Era - 1750 -1950 - Infections
- 2nd Era - 1950-2010 – Chronic Disease
- 3rd Era - 2010-Future – Health for All
1st Era of Modern Health
1750-1950

- Life expectancy of 47 years in 1900
- 1900-1950 life expectancy increases 21 years
- Dfn: Health as the Absence of Disease
- **Mechanism:** Infections/ Contact/ Single cause
- Approach: Medical Treatment + Public Health-Safety
- Finance: Insured Loss + Program Grants
- Delivery Mode: Clinic, Practice + Hospital, Public Health Department
- Goal: Reducing deaths
2nd Era of Modern Health Care
1950-2000+

- Life expectancy increases from 67 to 78 years
- Health as Absence of Disease, Disability and Dysfunction
  - Mechanism: Multiple risk factors, behaviors, lifestyle
- Approach: Chronic disease management, disease prevention, community care
- Finance: Pre-paid health benefits
- Delivery Mode: Health Maintenance Organization
- Goal: Prolonging Life
Life Span

Health Span

Performance Span

Health / functional Status

0 years

20 years

80 years

UCLA Center for Healthier Children, Families & Communities
Longitudinal research across the 3 eras of modern health care

- British birth cohort studies began in the transition from the 1\textsuperscript{st} to 2\textsuperscript{nd} era
  - Simple causal models $\rightarrow$ Multiple Risk models of disease causation
- Conceptually driven by the 2\textsuperscript{nd} era emphasis on understanding risks and interactions
- What the BBCS produce are a new understanding of how health develops
  - Complex and emergent
  - Product of multiple influences,
  - Multilevel, nested,
British Birth Cohort Studies

- 1946 National Survey of Health and Development
- 1958 National Child Development Study
- 1970 British Cohort Study
- 2000 Millennium Cohort Study
Growing up in Britain

CHANGING BRITAIN, CHANGING LIVES
THREE GENERATIONS AT THE TURN OF THE CENTURY
EDITED BY ELSA FERRL, JOHN BYNNER AND MICHAEL WADSWORTH

INSTITUTE OF EDUCATION
UNIVERSITY OF LONDON
British Birth Cohort Studies

- Large representative populations, selected at birth to ascertain true prevalence
- Prospective, well timed collections to minimize recall bias, and understand chronological sequencing
- Beginning at birth to understand how early life influence adulthood

From Ferri, Bynner, Wadsworth 2003
Responded to policy concerns of the day
- 1946 and 1958 cohorts provided data to evaluate the 1944 Education Act
- 1958 study continued because of concerns about educational attainment revealed in the Plowden Committee report

1960-70’s - Important Findings
- Role of early years in educational success
- Bio-psycho-social factors that influence cognition
- Risk, protective, resiliency models of behavioral outcomes

1980s - The emerging interest in the early origins of adult diseases
- Critical and sensitive periods of development
BBCS: Influence on Policy

- Plowden Committee
- Acheson Report
- Sure Start
- WHO Commission on Social Inequalities
BBCS: Children's Health

- Factors that influence health outcomes
  - Health visitors
- Social adversity and poor home circumstances on health
- Impact of health services on health outcomes
- Changing prevalence of health conditions
  - Obesity, asthma,
- Support for biological programming hypotheses
BBCS: Biological Programming

- Growth, before and after birth
  - Blood pressure
  - Cognition
  - Respiratory function
  - Body mass and obesity
  - Mental health
  - Menopause
  - More ....

- Contributing to the emergence of Developmental Origins of Adult Health and Disease (DOAHD)
- Lifespan theories – connect the dots
- Timing is important
  - Dynamics, plasticity,
- Life-course
  - Social cultural scaffolding that is created by families, schools, communities, workplace
  - Developmental Pathways
  - Developmental trajectories
- Historical embedding
Pathways to resilience

Responsive Communities (opportunities for participation, recognition and support)

Responsive Schools (developmentally appropriate curriculum, teaching & learning, school environment & ethos)

Responsive Parenting (appropriate care, stimulation, encouragement & monitoring)

Optimal brain development in utero and early childhood

Genetic factors

Healthy pregnancy, reduced maternal smoking, alcohol & drug misuse

Personal achievement, social competence and emotional resilience

Sense of self-efficacy & self-worth

Sense of social connectedness

Healthy beliefs and clear standards

Positive interaction with peers

Positive interaction with adults

Availability of +ve adult role models & engaging community activities

Reduced exposure to harmful drugs

Effective self regulation of emotion, attention & social interaction

Effective learning, communication & problem solving skills

Social and economic environments supportive to child rearing & education - especially absence of poverty and exposure to violence

Healthy nutrition in utero & throughout childhood & adolescence

Silburn, 2003
BBCS: Connecting the Dots

- Mechanisms that link early risk and adult health
  (Power, Hertzman, Kuh, Ben Shlomo)
  - Programming/ biological embedding
  - Cumulative mechanisms
  - Pathways
- Transitions and turning points
  - Children in care,
  - parental divorce
- Social & Cultural Change
  - Resources
  - Processes
  - Developmental expectancy
BBCS: Transforming Health Paradigms

- BBCS
  - Developmental Pathway across the life span
- Life Course Chronic Disease Epidemiology
- Developmental Origins of Adult Health and Disease
- Neuro-developmental
- Early intervention studies
Health

- Health is developmental
  - Health develops across the life course
  - Health development can be represented by health trajectories
  - Critical/ Sensitive periods
  - Gene - Environment – Interaction have different impacts during different periods
  - Macro and Micro pathways delineate how toxic environments and risky families get under the skin
“Children’s health is the extent to which individual children or groups of children are able or enabled to (a) develop and realize their potential, (b) satisfy their needs, and (c) develop the capacities that allow them to interact successfully with their biological, physical, and social environments.”

How risk reduction and health promotion strategies influence health development

FIGURE 4: This figure illustrates how risk reduction strategies can mitigate the influence of risk factors on the developmental trajectory, and how health promotion strategies can simultaneously support and optimize the developmental trajectory. In the absence of effective risk reduction and health promotion, the developmental trajectory will be sub-optimal (dotted curve). From: Halfon, N., M. Inkelas, and M. Hochstein. 2000. The Health Development Organization: An Organizational Approach to Achieving Child Health Development. The Milbank Quarterly 78(3):447-497.
Risk and protective factors

Risk Factors
- Child
- Family
- Community
- School

Protective Factors
- Child
- Family
- Community
- School

Outcome
- Negative vulnerability
- Positive resilience
Strategies to improve health development trajectories

- Ready to learn
- At Risk Trajectory
- Healthy Trajectory
- Delayed/Disordered Trajectory

Factors:
- Parent education
- Emotional Health
- Literacy
- Reading to child
- Appropriate Discipline
- Health Services
- Family Discord
- Poverty
- Lack of health services
- Pre-school

Age:
- Birth
- 6 mo
- 12 mo
- 18 mo
- 24 mo
- 3 yrs
- 5 yrs

Developmental stages:
- Early Infancy
- Late Infancy
- Late Toddler
- Late Preschool
Developmental Trajectories are Mutable and Dynamic

- Genes are not destiny
- Developmental modulation influences trajectories
- Epigenesis implies that the external environment alters internal environment that internal environment alters gene expression
- Gene expression is mediated by the biological, social, physical environments
- Developmental process is not linear
LCHD and G-E interactions

- Serotonin Receptor 2A + maternal nurturance = protection from depression
- Dopamine Transporter Gene + Maternal Smoking = hyperactivity, impulsivity, and oppositional behaviors (Kahn J Peds 2003)
- Serotonin Transporter Promoter + family stress = depression
Variations in Functional Trajectories

- Developmental function vs. Age
Transitions and Turning Points of Social Emotional Development

Risk Factor

Entry into Pre-school

Entry into Child Care

Protective/Promoting Factors
Variations in Functional Trajectories

Risk Factors

Protective, promoting factors

Pre-school entry
How are the Children?

Current Status of Children in the U.S.
Steady Progress in Childhood Morbidity for traditional medical conditions
  - Many indicators show improvement
    - Mortality, morbidity, trends improving

Increasing Rates of chronic conditions, especially mental health, developmental and behavioral conditions, & Obesity

Increasing disparities
EXHIBIT 7
U.S. Mortality Rates In Children, By Age Group, 1979–2000

Deaths per 100,000 children

100

80

60

40

20

0


Ages 15–19

Ages 1–4

Ages 10–14

Ages 5–9

DISCHARGE RATE OF PATIENTS 1-14 YEARS OLD FOR SELECTED DIAGNOSES: 1985-2000
Source (II.9): National Center for Health Statistics
Changing Pattern of Childhood Morbidity

- Increase in chronic health problems (10-14%)
- Greater recognition of mental health problems (15-20%)
- Greater appreciation of role and impact of developmental health problems – learning, language (10-17%)
Children Aged 10-17 Years Who Are Overweight, by Family Income: 2003

Source (I.2): Centers for Disease Control and Prevention, National Center for Health Statistics, National Survey of Children’s Health

% of Population Overweight

- 0-99% FPL: 22.4%
- 100-199% FPL: 19.0%
- 200-399% FPL: 13.7%
- 400% or More FPL: 9.1%
The Health of Children & Youth

4-6% Severe Disabilities

12-16% Special Health Care Needs

30-40% Behavioral, Mental Health Learning Problems

50-60% Good Enough

What % are thriving?

30%?

40%?

50%?
The National Children’s Study:
The United States’ largest long-term study of children’s health
The National Children’s Study

- Longitudinal study of children, their families, and their environment (over 21 years or longer, from before birth)
- Environment defined broadly (chemical, physical, behavioral, social, cultural)
- Approximately 100,000 children included to study important but less common outcomes
Study Origins

- President’s Task Force on Environment and Health Risks to Children – 1998
  - Co-chairs Sec. HHS & Adm. EPA + 7 other cabinet member
  - Charge: National strategies to control environ. risks
  - Finds - **Bold study** needed to identify effects or ensure safety

- Children’s Health Act of 2000: “..authorize NICHD to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development”
Converging factors underlying study development

- Increased vulnerability of children
- Many identified environmental exposures with concerns about toxic and other adverse effects in children
- Diseases and developmental conditions with possible environmental causes or contributions
- Numerous experiences of adverse effects of environmental exposures on children’s health and development
Examples of Environmental Effects in Children

- Lead exposure and neuropsychological Development
- Prenatal alcohol exposure and malformations with developmental delay – FAS
- Ionizing radiation and malignancy – leukemia, thyroid carcinoma
- Prenatal Hg and developmental delay
- Prenatal DES and vaginal cancer, male reproductive tract abnormalities
- Thalidomide and limb defects
Some exposures of potential concern

- Chemical products – 15,000 high production, many in households, air, water, food
  - Pesticides – Organophosphate, Pyrethroids
  - Solvents – alcohol, toluene, other

- Food Additives – glutamate, aspartame, dyes

- Infection in early life – H. pylori – gastritis; C. pneumoniae – coronary vascular disease

- Head trauma – mild/moderate, age 0-14, 4/1,000

- Witness violence – 3.3 million children

- Neighborhoods – cohesion, collective efficacy

- Poverty – 18% of children in poverty
### Priority Health Outcomes/Exposures

#### Priority Exposures

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<th>Physical Environment</th>
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#### Priority Health Outcomes

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<th>Neurodevelopment &amp; Behavior</th>
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<th>Examples</th>
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<td>Obesity, Diabetes, altered puberty</td>
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Study Concepts

- Hypothesis driven
- Exposure begins with pregnancy
- Has power to study high priority conditions ($n\sim100,000$)
- Gene environment interaction
- Consortium of Federal Agencies
- Public-private partnerships
- National resource for future studies
Hypotheses necessary for framing the study

- 29 main hypothesis (see NCS website)
- Assure answers to “big issue” questions
- Hypotheses required for costly elements
- **Requires and measurable with sample ~100,000**
- Evolving with the science
- Help to frame protocol development
Examples of Hypotheses defining questions

- What are the health and developmental effects of persistent low level chemical exposures?
- How is asthma incidence and severity influenced by the interaction of early life infection and air quality?
- Is pre-term birth caused by intrauterine inflammation and infection?
- Does impaired maternal glucose metabolism during pregnancy cause obesity in children?
- How does high level exposure to media content in infancy affect development and behavior in children?
- Does pre-and post-natal exposure to endocrine-active environmental agents alter age at onset, duration, and completion of puberty?
### Population Size for Selected Outcomes

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<td>10/10K</td>
<td>157K</td>
<td>77K</td>
<td>47K</td>
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<td>313K</td>
<td>153K</td>
<td>94K</td>
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<td>78K</td>
<td>38K</td>
<td>23K</td>
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<td>800/10K</td>
<td>1.8K</td>
<td>0.9K</td>
<td>0.5K</td>
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<td>690/10K</td>
<td>2K</td>
<td>1K</td>
<td>0.6K</td>
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<td>Hospitalizations (&lt;15)</td>
<td>27.7/10K</td>
<td>56K</td>
<td>28K</td>
<td>17K</td>
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*prevalence
How will Study size produce results not otherwise available?

- Exposures for “big issue” low frequency outcomes
  - Autism
  - Diabetes
  - Still birth
  - Birth defects, etc.

- Sub-groups and multi-factor interactions
  - Obesity
  - Asthma
  - Behavior, etc.
Sampling and Center strategies

- National probability sample important
  - Exposure-outcome relationship representative of the U.S. population
  - Important exposures with varied and unknown distributions are not missed
  - Clustered for community attributes & logistics

- Centers of excellence important
  - Broad scientific input
  - Measures require center based expertise and facilities
  - Community engagement and identity important for recruitment and retention

- Probability sample by Centers
  - Unique combination
  - Requires flexibility and adaptation of center to the scientific design
  - Requires support and guidance by coordinating center
National Children’s Study Sample

- All Births in the Nation
  - Sample of Study Locations: 105 Locations
  - Sample of Study Segments: Selection of neighborhoods
  - Sample of Study Households: All or a sample of households within neighborhoods
  - Sample of Study Women: All eligible women in the household

- ~4 million births in 3,141 counties

National Children’s Study Locations

Map Legend
- Wave 1 Locations
- Vanguard/Wave 1 Locations
- Wave 2 Locations
- Wave 3 Locations
- Wave 3 Locations Not Awarded

October 2008
Who will be enrolled?

- **Household recruitment**
  - Women who are in the first trimester of pregnancy
  - Women who are planning a pregnancy
  - Women of child bearing age who are not planning pregnancy but could become pregnant during the enrollment period

- **Supplemental recruitment**
  - Prenatal care providers
  - Community based recruitment of eligible women
## Proposed Schedule of Visits for Core Protocol

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<tr>
<th>Clinical Setting</th>
<th>1st Trimester</th>
<th>2nd Trimester UTZ</th>
<th>3rd Trimester</th>
<th>Delivery Visit</th>
<th>6 months</th>
<th>12 months</th>
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<tr>
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<td>3 years</td>
<td>5 years</td>
<td>8 years</td>
<td>12 years</td>
<td>16 years</td>
<td>20 years</td>
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- **Home**
- **Clinical Setting**
Los Angeles- Ventura Study Center

- 4000 Children in Los Angeles, 1000 in Ventura
- LA - 56 different neighborhoods
  - Malibu to South Central Los Angeles
- LA - 80 different birth hospitals
- LA- 30-50 Ultrasound Sites
Adjunct studies: opportunity for innovative projects

- Involve a portion of the sample using some NCS infrastructure and data to address additional or in-depth questions

- Examples:
  - Genomic analysis of subgroup specimens for targeted gene-environment interactions
  - Functional neuro-imaging of exposed subgroup for mechanism of effect on child development
Formative Studies

- To develop more effective and efficient ways of collecting data
- To test additions and changes in the protocol
- To examine the feasibility of data collection in “natural settings”
- To gather additional information that will improve the overall organization, execution of the study.
Use and access to data

- Maximum use and publication will be a guiding principle
- Planned analyses of core hypotheses by the community of NCS investigators
- Public use data sets by Study phases
  - Totally anonymous limited data set with open access
  - De-identified with requirements for access
  - Highly restricted with rigorous safeguards
- For Federal programs and missions
What could be new and innovative?

- Emphasis not only on disease but on measures of positive health and development
- Ability to incorporate multi-level and spatial analyses
- Ability to focus on gene-environment interactions at critical turning points in development
- Ability to link NCS data to existing data sets, and ongoing data collection schemes
How are the BBCS and New Life Course Health Development Paradigm Transforming Health and Health Care?

The Emerging Future
The Emerging Future

- New Era of Health and Health Care
- New approaches to old problems
- Imperative for Transdisciplinary Research Strategies
- More Integrated Service Delivery and Policy
Three Era’s of Health Care

- 1<sup>st</sup> Era - 1750 -1950 - Infections
- 2<sup>nd</sup> Era - 1950-2010 – Chronic Disease
- 3<sup>rd</sup> Era - 2010-Future – Health for All
3rd Era of Modern Health Care
2008 -?

- Life expectancy 78>>>85+
- Health as positive capacity to achieve life’s goals
- Mechanism: developmental processes, social networks, psychosocial relations, gene – environment transactions across the life span
- Disparities: Developmental programming, cumulative, pathways
- Approach: Life Course Health Management and Health promotion
- Finance: Investment in health capital
- Delivery Mode: Health Development Org. run by Health Outcomes Trust
- Goal: Health for all
The Evolving Health Care System

The First Era (Yesterday)
- Focused on acute and infectious disease
- Germ Theory
- Medical Care
- Insurance-based financing
- Reducing Deaths

Health System 1.0

The Second Era (Today)
- Increasing focus on chronic disease
- Multiple Risk Factors
- Chronic Disease Mgmt & Prevention
- Pre-paid benefits
- Prolonging Disability free Life

Health System 2.0

The Third Era (Tomorrow)
- Increasing focus on achieving optimal health status
- Complex Developmental Pathways
- Investing in population-based prevention
- Producing Optimal Health for All

Health System 3.0
### 3.0 Operating Logic

<table>
<thead>
<tr>
<th></th>
<th>Old Operating Logic</th>
<th>New Operating Logic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition of Health</strong></td>
<td>Absence of disease &amp; disability</td>
<td>Health is a positive concept emphasizing social and personal resources, as well as physical capacities (Ottawa, 1986)</td>
</tr>
<tr>
<td><strong>Goals of Health System</strong></td>
<td>Health maintenance &amp; prolonging life of individual</td>
<td>Optimizing population health</td>
</tr>
<tr>
<td><strong>Client Model</strong></td>
<td>Individual</td>
<td>Individual, community &amp; population</td>
</tr>
<tr>
<td><strong>Model of Health Production / Disease Causation</strong></td>
<td>Biomedical</td>
<td>Biopsychosocial</td>
</tr>
<tr>
<td><strong>Intervention Approach</strong></td>
<td>Diagnosis &amp; treatment</td>
<td>Emphasize disease prevention, health promotion and optimization of function as core components</td>
</tr>
<tr>
<td><strong>Time Frame</strong></td>
<td>Episodic</td>
<td>Lifespan</td>
</tr>
</tbody>
</table>
3.0 Care: Moving Upstream

1 = current practice
2 = current capability
3 = future capability

**Risk Assessment for Prospective Health**

Risk assessment decision support

- **Symptoms**
  - Low risk
  - High risk
  - Early chronic
  - Late chronic
- **Cost**

**Years**

- **Personalized health plan**
  - **Health Promotion Plan**
    - Wellness education and Internet and health provider guided planning for all
  - **Risk modification**
    - Wellness education and Internet and health provider guided planning for all
  - **Disease management**
    - Individual-focused; integrated provider systems. Focus on quality of life and palliation at appropriate late stages

**Source:** Snyderman R. AAP presidential address: the AAP and the transformation of medicine. Journal of Clinical Investigation. 2004;114(8):1169-1173 (suppl)
The Emerging Future

- New Era of Health and Health Care
- **New approaches to old problems**
- Transdisciplinary Strategies
- More Integrated Service Delivery and Policy
U.S. INFANT MORTALITY RATES BY RACE OF MOTHER: 1980-2000*

Source (II.4): National Center for Health Statistics

*preliminary data

**Includes the ethnic classification of Hispanic.
LCHD and Birth Outcomes

Reproductive Potential

Age

White

African American

Pregnancy
LCHD and Birth Outcomes

Reproductive Potential vs. Age

- White
- African American

Pregnancy
Life Course Health Development

- Poor Nutrition
- Stress
- Abuse
- Tobacco, Alcohol, Drugs
- Poverty
- Lack of Access to Health Care
- Exposure to Toxins

Age: 0, 5

- White
- African American

Poor Birth Outcome

Puberty

Pregnancy
LCHD: AA – White Birth outcomes

- Prenatal Care
- Early Intervention
- Primary Care for Children
- Primary Care for Women
- Prenatal Care
- Internatal Care
- Poor Birth Outcome

Age 0 5

Puberty
Pregnancy

White
African American
The Emerging Future

- New Era of Health and Health Care
- New approaches to old problems
- Transdisciplinary Strategies
- More Integrated Service Delivery and Policy
Comparisons of Disciplinary, Multidisciplinary, Interdisciplinary, and Transdisciplinary Research Paradigms

Source: Aday LA. Reinventing Public Health. 2005; p20
Mental Capital and Wellbeing:
Making the most of ourselves in the 21st century

EXECUTIVE SUMMARY
Appendix B: Synthetic view of the mental capital trajectory and factors that may act upon it

- Environment
  - Home/Family environment
  - School environment
  - Media/Information environments

- Mental Capital
  - Early life experiences
  - Parenting skills
  - Positive parenting style
  - Parental modelling
  - Knowledge, attitudes, and aspirations towards parenting
  - Education, Employment, Income, Occupational status, Social status
  - Physical health, behavioural risk factors

- Transport
  - Self-controlled peer resistance
  - Impulsivity
  - Drug and alcohol abuse

- Social support
  - Cognitive resilience and coping skills
  - Learning and executive function
  - Episodic and working memory

Technological interventions
- Early assessment and treatment of age-related disorders
- Cognitive training
- Pharmacological cognitive enhancement
- Stem cells in neural regeneration and adult neurogenesis
- Nutritional strategies
- Cognitive prosthetics

Biological factors
- Nutrition
- Sleep
- Exercise

School
- Footprint programming
- Early development
- Childhood

Work
- Chronic inflammation
- iNOS (3-phosphorylated fatty acids, folate, vitamin B6, and cognitive function)

Retirement
- Later life
- Brain atrophy and white matter lesions
- Accumulated damage to cells and tissues

Understanding lifetime factors and experiences towards aging, ageism, and social marginalization.
The Emerging Future

- New Era of Health and Health Care
- New approaches to old problems
- Transdisciplinary Strategies
- More Integrated Service Delivery and Policy
Trajectory Optimizing Service Linkage Pathway
Conclusion

- BBCS have worked at micro, macro, meta historical level to transform research, programs, and policy
- BBCS provided the foundation for a major paradigm shift in health and health care
  - LCHD
  - Health 3.0
- NCS has the opportunity to write the next chapter
- Spirit of Neville Butler
  - Innovate, Advocate, Translate, Invest
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