Nutrition and Cardiovascular Disease

Acute and General Medicine for the Physician
Royal College of Physicians
London, October 2015

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University of Southampton
Eradicate extreme poverty and hunger

Achieve Universal Primary Education

Promote Gender Equality and Empower Women

Reduce Child Mortality

Improve Maternal Health

Combat HIV, AIDS Malaria and other Diseases

Ensure Environmental Sustainability

Develop a Global Partnership for Development

To achieve these goals, poorer countries pledged to improve policies and governance and increase accountability to their own citizens; wealthy countries pledged to provide the resources.
Sustainable Development Goals 2015-2035

http://www.sustainabledevelopment2015.org/
Double Burden of Malnutrition
Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

Figure 7: The 25 leading level 3 global risk factors for DALYs in both sexes combined in 2000 and 2013

<table>
<thead>
<tr>
<th>Mean rank (95% UI)</th>
<th>2000 leading risks</th>
<th>2013 leading risks</th>
<th>Mean rank (95% UI)</th>
<th>All age median % change</th>
<th>Age-standardised median % change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-0 (1-1)</td>
<td>Childhood undernutrition</td>
<td>1 High blood pressure</td>
<td>1-0 (1-1)</td>
<td>20% (15 to 26)</td>
<td>-13% (-16 to -9)</td>
</tr>
<tr>
<td>2-0 (2-2)</td>
<td>High blood pressure</td>
<td>2 Smoking</td>
<td>2-6 (2-4)</td>
<td>5% (-1 to 11)</td>
<td>-23% (-28 to -19)</td>
</tr>
<tr>
<td>3-3 (3-4)</td>
<td>Smoking</td>
<td>3 High body-mass index</td>
<td>2-8 (2-5)</td>
<td>26% (22 to 31)</td>
<td>-7% (-11 to -5)</td>
</tr>
<tr>
<td>4-0 (3-6)</td>
<td>Unsafe water</td>
<td>4 Childhood undernutrition</td>
<td>4-2 (3-6)</td>
<td>-45% (-51 to -39)</td>
<td>-50% (-55 to -44)</td>
</tr>
<tr>
<td>5-2 (4-8)</td>
<td>High body-mass index</td>
<td>5 High fasting plasma glucose</td>
<td>4-6 (3-6)</td>
<td>31% (25 to 36)</td>
<td>-4% (-8 to 0)</td>
</tr>
<tr>
<td>6-9 (5-11)</td>
<td>Alcohol use</td>
<td>6 Alcohol use</td>
<td>6-9 (5-9)</td>
<td>6% (2 to 11)</td>
<td>-17% (-20 to -13)</td>
</tr>
<tr>
<td>7-6 (5-11)</td>
<td>Household air pollution</td>
<td>7 Household air pollution</td>
<td>9-1 (8-12)</td>
<td>-10% (-21 to 2)</td>
<td>-28% (-38 to -18)</td>
</tr>
<tr>
<td>7-9 (5-11)</td>
<td>High fasting plasma glucose</td>
<td>8 Unsafe water</td>
<td>10-4 (8-14)</td>
<td>-37% (-44 to -30)</td>
<td>-43% (-49 to -37)</td>
</tr>
<tr>
<td>9-2 (6-12)</td>
<td>Unsafe sanitation</td>
<td>9 Unsafe sex</td>
<td>10-8 (8-13)</td>
<td>-3% (-11 to 7)</td>
<td>-20% (-26 to -11)</td>
</tr>
<tr>
<td>11-5 (8-14)</td>
<td>Unsafe sex</td>
<td>10 Low fruit</td>
<td>10-8 (7-16)</td>
<td>7% (1 to 14)</td>
<td>-22% (-26 to -16)</td>
</tr>
<tr>
<td>12-0 (6-17)</td>
<td>Suboptimal breastfeeding</td>
<td>11 High sodium</td>
<td>11-4 (5-20)</td>
<td>15% (7 to 24)</td>
<td>-16% (-22 to -10)</td>
</tr>
</tbody>
</table>


Figure 1: The 25 leading GBD level 3 causes of years of life lost (YLLs) in England, both sexes combined, 1990, 2005, and 2013, with age-standardised median percent change

<table>
<thead>
<tr>
<th>Mean rank (95% UI)</th>
<th>1990 leading causes</th>
<th>2005 leading causes</th>
<th>Mean rank (95% UI)</th>
<th>Age-standardised median percentage change 1990–2005</th>
<th>2013 leading causes</th>
<th>Mean rank (95% UI)</th>
<th>Age-standardised median percentage change 2005–2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:0 (1-1)</td>
<td>Ischaemic heart disease</td>
<td>1:0 (1-1)</td>
<td>-46% (-47 to -39%)</td>
<td>Ischaemic heart disease</td>
<td>1:0 (1-1)</td>
<td>-22% (-26 to -17%)</td>
<td></td>
</tr>
<tr>
<td>2:0 (2-2)</td>
<td>Cerebrovascular disease</td>
<td>2:1 (2-3)</td>
<td>-32% (-35 to -25%)</td>
<td>Lung cancer</td>
<td>2:1 (2-3)</td>
<td>0% (-8 to 7%)</td>
<td></td>
</tr>
<tr>
<td>3:0 (3-3)</td>
<td>Lung cancer</td>
<td>2:9 (2-3)</td>
<td>-21% (-25 to -19%)</td>
<td>Cerebrovascular disease</td>
<td>2:9 (2-3)</td>
<td>-14% (-19 to -9%)</td>
<td></td>
</tr>
<tr>
<td>4:2 (4-5)</td>
<td>COPD</td>
<td>4:2 (4-5)</td>
<td>-1% (-19 to 3%)</td>
<td>COPD</td>
<td>4:3 (4-6)</td>
<td>-5% (-12 to 2%)</td>
<td></td>
</tr>
<tr>
<td>4:8 (4-5)</td>
<td>Lower respiratory infections</td>
<td>4:8 (4-5)</td>
<td>-11% (-15 to 2%)</td>
<td>Lower respiratory infections</td>
<td>5:3 (4-6)</td>
<td>9% (-2 to 20%)</td>
<td></td>
</tr>
<tr>
<td>5:6 (6-7)</td>
<td>Colorectal cancer</td>
<td>5:6 (6-7)</td>
<td>20% (8 to 34%)</td>
<td>Colorectal cancer</td>
<td>7:0 (7-8)</td>
<td>0% (-7 to 6%)</td>
<td></td>
</tr>
<tr>
<td>6:9 (6-7)</td>
<td>Breast cancer</td>
<td>7:1 (7-8)</td>
<td>-18% (-21 to -16%)</td>
<td>Breast cancer</td>
<td>8:0 (7-8)</td>
<td>-12% (-19 to 0%)</td>
<td></td>
</tr>
<tr>
<td>8:3 (8-9)</td>
<td>Alzheimer’s disease</td>
<td>7:9 (6-8)</td>
<td>-18% (-22 to -15%)</td>
<td>Self-harm</td>
<td>9:1 (9-10)</td>
<td>-13% (-24 to -3%)</td>
<td></td>
</tr>
<tr>
<td>8:8 (8-10)</td>
<td>Self-harm</td>
<td>9:0 (9-9)</td>
<td>-29% (-31 to -15%)</td>
<td>Pancreatic cancer</td>
<td>10:6 (10-12)</td>
<td>8% (1 to 15%)</td>
<td></td>
</tr>
<tr>
<td>9:9 (9-10)</td>
<td>Road injuries</td>
<td>10:4 (10-11)</td>
<td>-33% (-35 to -30%)</td>
<td>Road injuries</td>
<td>10:4 (10-11)</td>
<td>-33% (-35 to -30%)</td>
<td></td>
</tr>
</tbody>
</table>
Risk Factors

Cardiovascular Disease
Chronic Non-communicable Diseases

Smoking
Hypertension
Obesity
Diabetes
Sixty-sixth session
Agenda item 117
Follow-up to the outcome of the Millennium Summit

Draft resolution submitted by the President of the General Assembly

Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases

The General Assembly,

Adopts the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases annexed to the present resolution.
Life Course: the proposed causal links

Resilience: capacity. Allostatics load: environmental stressors
Hillary Clinton Launches 1,000 Days Movement
Conception to 2 years of age
September 2010

Double Burden of Malnutrition:
Malnutrition in All its Forms:
Underweight, Overweight, Micronutrient Deficiencies

United Nations: Scaling Up Nutrition (SUN)
Barker Hypothesis
Fetal Origins Hypothesis of Chronic Disease

Disorders originate through Developmental Plasticity

Poor nutrient exposure: early life (fetus, infant, early childhood)

Permanent change in structure and function:
  - tissues and organs

Vulnerable period: timing, intensity, duration
Barker Hypothesis

Coronary heart disease

Standardised mortality ratios (SMR) in 10141 men & 5585 women

Variable risk across the range of weight at birth & at age one year, which is not a feature of the extremes of the ranges, very low or very high.

BMJ 1993;307:1519-24
Barker hypothesis:
Fetal Origins of Chronic Disease:

Coronary heart disease, Stroke, Hypertension

Type 2 diabetes, Bone Health

Cancers, Mental Health

Developmental Model for Disorders
Key features of the epidemiological studies

• graded inverse association between markers of fetal growth and specific adult degenerative conditions,

• associations seen for both sexes, reproduced in a variety of studies in other populations

• similar pattern of association with the known adult physiological risk factors for these conditions

• the effects of smaller size at birth are not a consequence of prematurity, nor can they be explained by confounding influences acting in adult life
Evidence from animal studies

Modest dietary manipulation during pregnancy leads to reproducible change in a wide range of functions

- effects specific, not generalised
- fundamental changes in metabolic competence
- changes in growth, one manifestation
Animal models

altered growth fetus and placenta
altered body composition
sexual dimorphism

Changed metabolic function

- blood pressure
- glucose tolerance
- appetite control
- obesity
- immune dysfunction
- inflammatory changes
- behaviour
Fetus:

reset of central set-point for key hormonal axes

hypothalamo - pituitary-adrenal

growth hormone – IGF – insulin

thyroid axis

sex steroid axis

- response to diet
- response to stressors
Systolic Blood Pressure
Maternal Exposure to Protein Diet

Systolic Blood Pressure, mm Hg

6% 9% 12% 18%

Casein content of maternal diet during pregnancy

Systolic blood pressure, mm Hg
Glycine and folic acid supplementation prevent hypertension

Blood pressure at 4 weeks in females

Maternal diet

Folic acid supplemented

Jackson et al. 2002, Torrens et al. 2006
Epigenetic Effect: Hepatic Glucocorticoid Receptor: methylation of promoter region of gene and gene expression
Maternal dietary folic acid interacts with protein, to modulate in offspring the methylation of the promoter region of DNA leading to altered gene expression for:

**PPAR**
- energy/macronutrient partitioning or risk of central adiposity.

**Glucocorticoid receptor**
- susceptibility to stressful experience

Dietary modulation, epigenetic transmission of response

Lillycrop et al, J Nutr 2005, 135, 1382-1386
Structure and function inextricably linked at every level of organization

Molecular:
  genetic, epigenetic

Cellular:
  membrane structure and function
  receptor function
  signalling, replication, differentiation

Tissue, organ
  Head circumference: brain
  Renal size: nephron number
  Abdominal circumference: hepatic architecture

Body shape:
  height, lean, adipose

Structure/function
Growth and Disease Susceptibility

Extent and pattern of growth and development;

Set *metabolic capacity*:

Determines magnitude of *resilience*

*Response* to nature and magnitude of allostatic load

Determines level and expression of risk

Vulnerability to specific disease(s)
Changes in functional capacity with age.
Changes in functional capacity with age

Maximum functional capacity
Changes in functional capacity with age

Minimum functional capacity for health
Changes in functional capacity with age

Reserve functional capacity

Functional capacity

Age, years

Age, years
Changes in functional capacity with age

Minimum functional capacity for health

Ill-health
Cumulative metabolic experience - epigenetics

- gene
- mother/father
- embryo
- preconception
- fetal
- pregnancy
- infant
- childhood
- adolescent
- adulthood

programming

growth

shape and size

body composition

lifestyle

HEALTH AND WELLBEING or DISEASE
Evidence for dietary changes over the past 25 years


Salt: SACN Report 2003 (salt and health)


Sugar: 2015
Sustainable Development Goals

Capacity: capability, mass

Increases with growth/maturation

Decreases with aging/misuse

Resilience: reserve capacity.

Challenge: environmental allostatic load

Risk – reduced capacity relative to allostatic load

Response:
  enhance capacity,
  reduce allostatic load to within capacity to cope