

"Evidencias de estudios de cohorte al nacimiento sobre el desarrollo de Enfermedades Crónicas No Transmisibles (ECNT)"

Carlos Grandi, *MD,MS,PhD*
Perinatal Epidemiology

Environment Special:
The oceans—why 70%
of our planet is in danger

The Facebook Movie:
The secret history of
social networking

TIME



**How the
first nine
months
shape
the rest
of your life**

The new science
of fetal origins

BY ANNIE MURPHY PAUL

LOVE

As últimas descobertas da medicina sobre como os nove meses importantes são decisivos para uma vida mais saudável

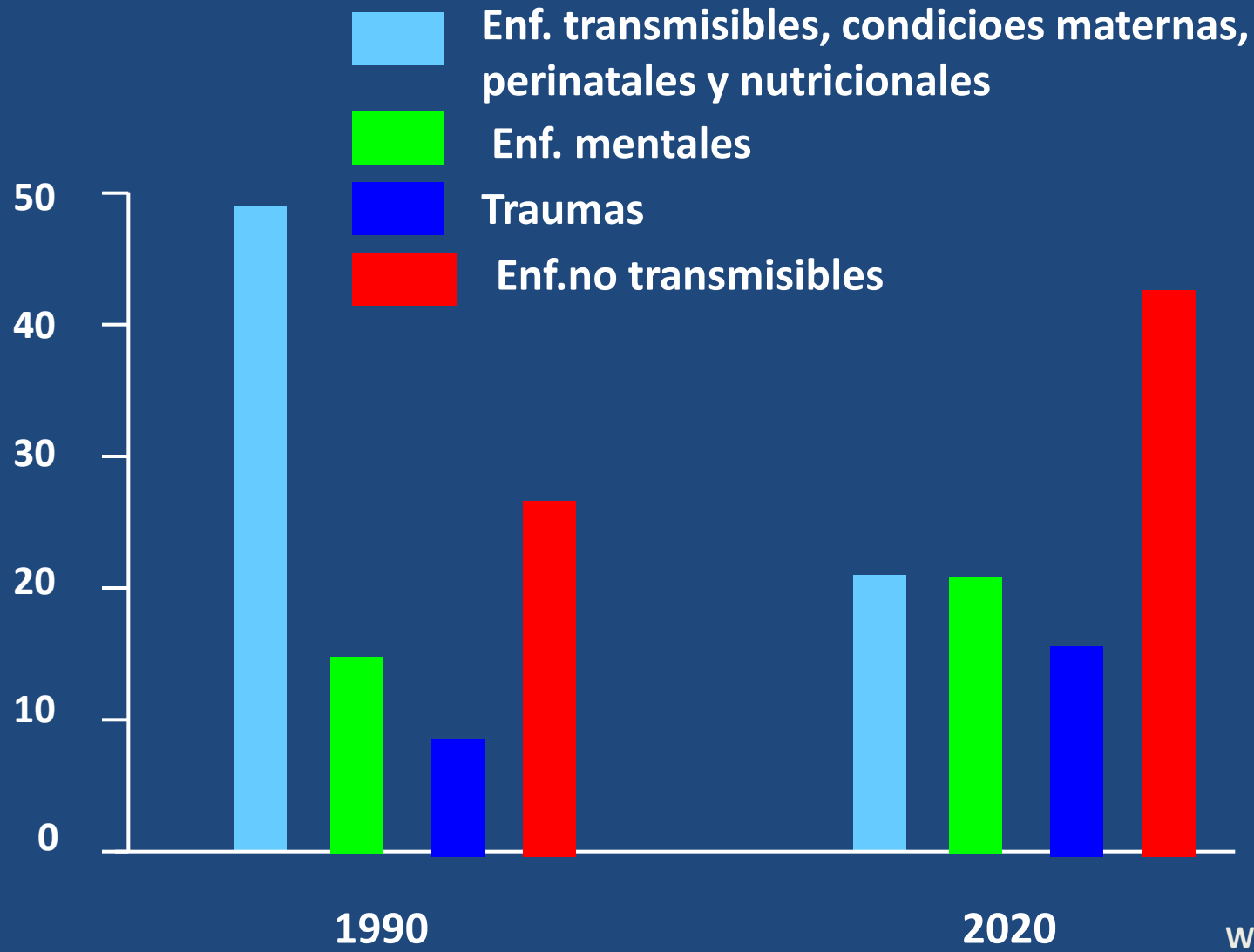
A FONTE DA SAÚDE

Saber usar esse período para prevenir doenças como diabetes, depressão e câncer

- Individuos viven mas tiempo → más posibilidad de enfermarse
- Como consecuencia, la elaboración de **nuevas líneas de causalidades** son necesarias en una perspectiva de esclarecer las nuevas asociaciones entre:

eventos precoces & resultados tardios

Carga de Enfermedades en Países en Desarrollo



Hipótesis de Barker



Condiciones adversas intra-uterinas y durante
la infancia ↑ el riesgo de enfermedades
cardiovasculares

JORNADA DE PERINATOLOGIA
HONORAR AL
PROFESOR
DR. JACINTO HALAC
AÑO: 7-4-2004
EL FUTURO DE LA
PERINATOLOGIA
CONDICIONES FETALES
EN LA INFERMEDAD
ADULTA

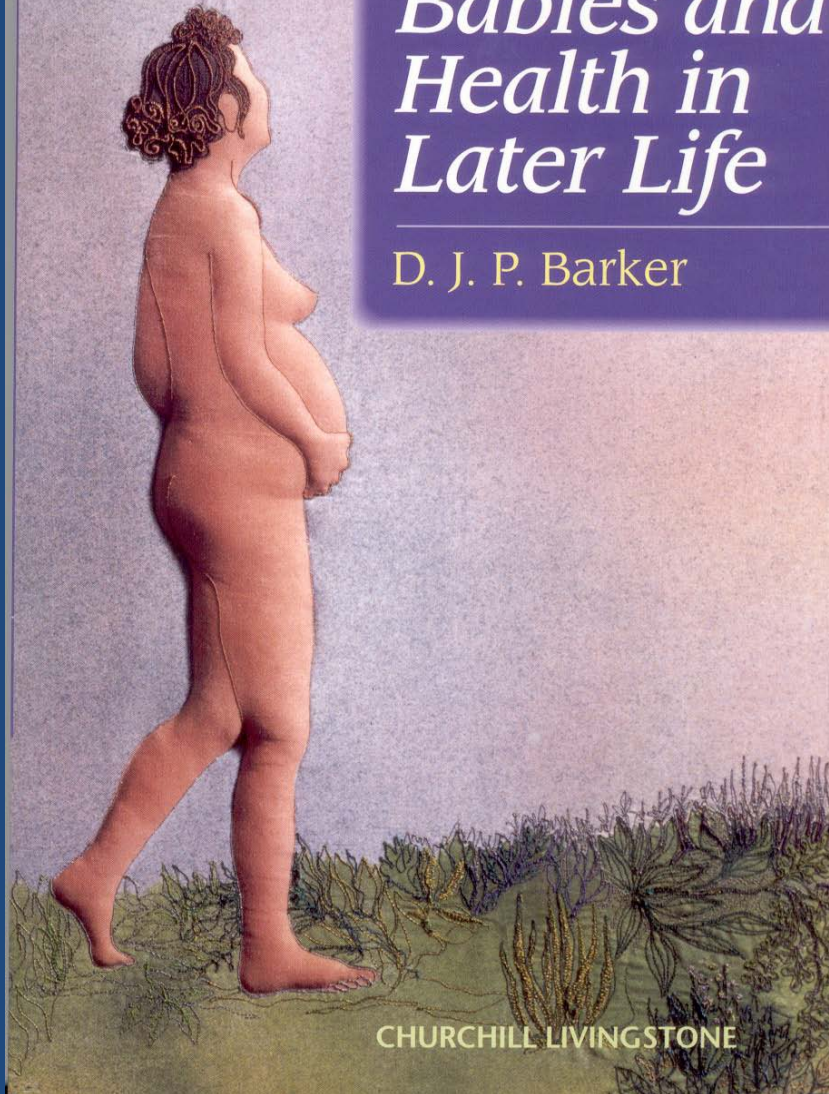


Jornada de Perinatología en honor del Prof. Halac - Córdoba, 2004

SECOND EDITION

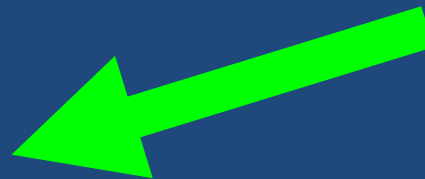
Mothers, Babies and Health in Later Life

D. J. P. Barker



CHURCHILL LIVINGSTONE





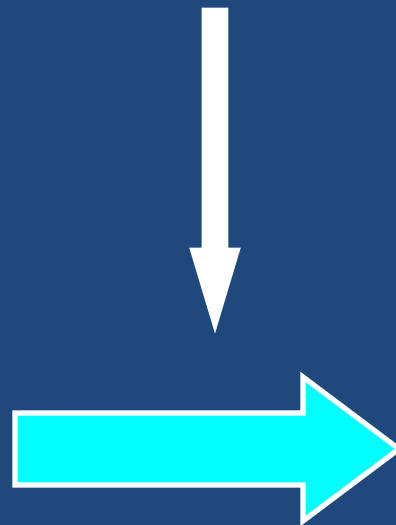
Quando adulto + propenso a:

- Hipertension arterial
- Diabetes Tipo 2
- Alteración de lípidos
- ↓ densidad ósea
- Arterias menos elásticas
- Depresión

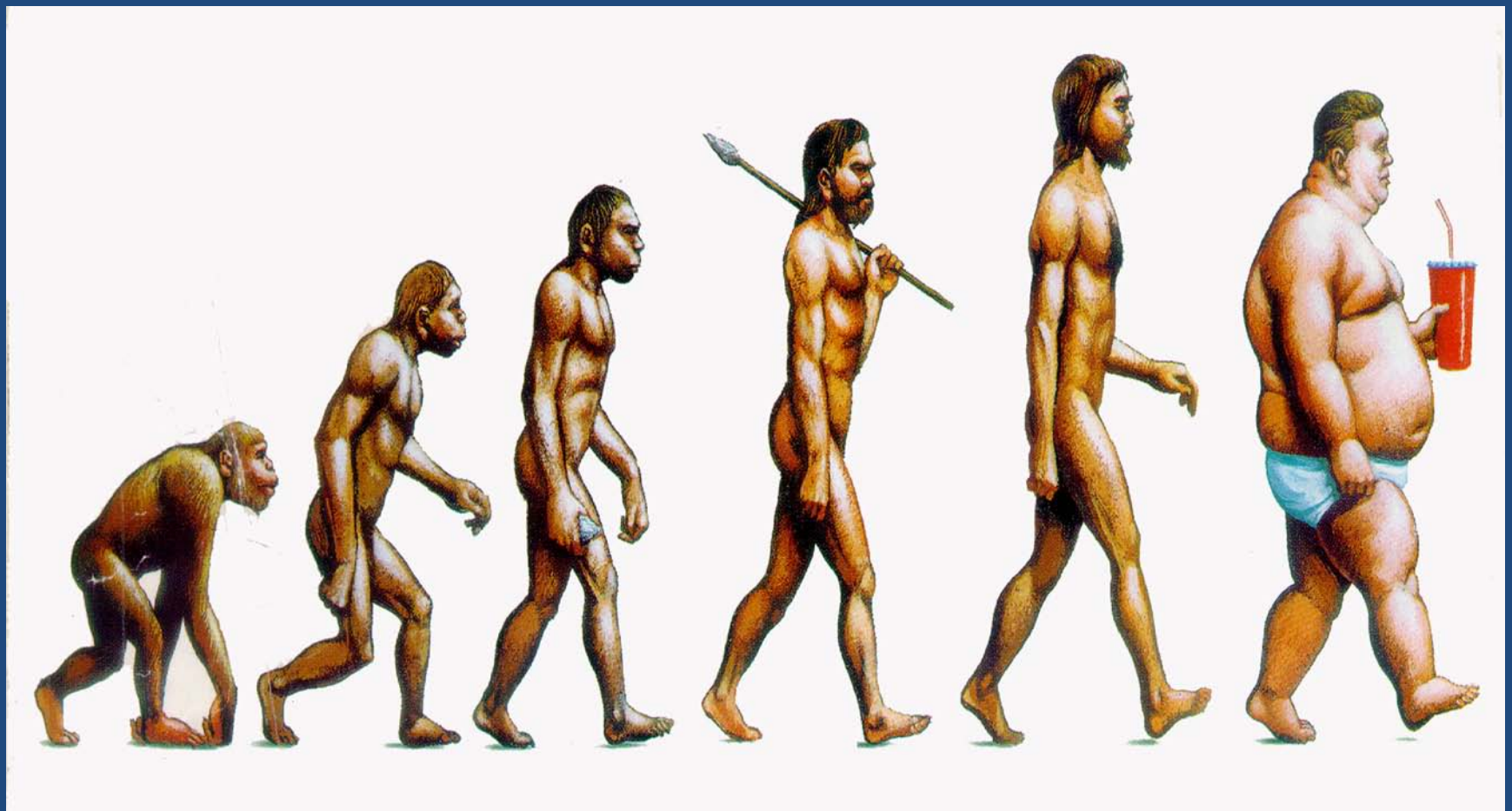
Hipótesis de Barker para ECV

**Mala Nutrición, Salud y
Desarrollo**

Niñas y
Mujeres
Jovenes



↑ Mortalidad por
ECV en la próxima
generación



SEDENTARISMO

EXPOSICION A AGENTES SENSIBILIZANTES

HÁBITO DE FUMAR

Justificación

Mala nutrición intra-útero y/o
en la lactancia



Cambios:

- fisiológicos
- metabólicos
- estructurales

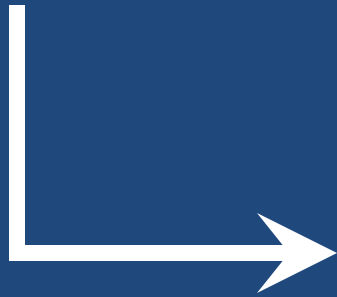


Tendencia a ECV y
Hemorragia
Cerebral

Programación Normal

Ambiente Nutricional,
Hormonal y Metabólico
en el Útero

Estructuras y
Funciones Normales
de los Órganos



Programa



El "Programming"



Sub-nutrición Materna

Otras
Anormalidades

Sub-nutrición Fetal

Alteración del
funcionamiento
hepático

↓ Células β

Resistencia a
Insulina

Desarrollo vascular
anormal

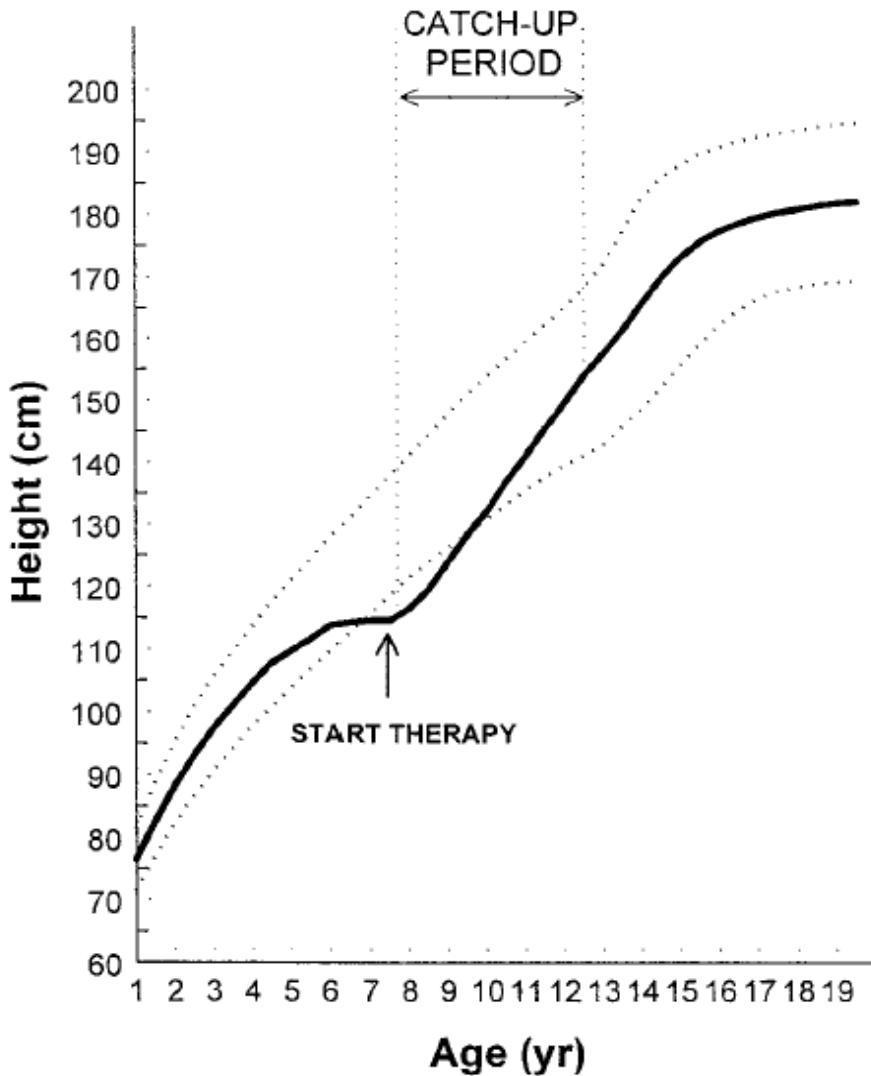
Hiperlipidemia

DM Tipo 2

Hipertensión

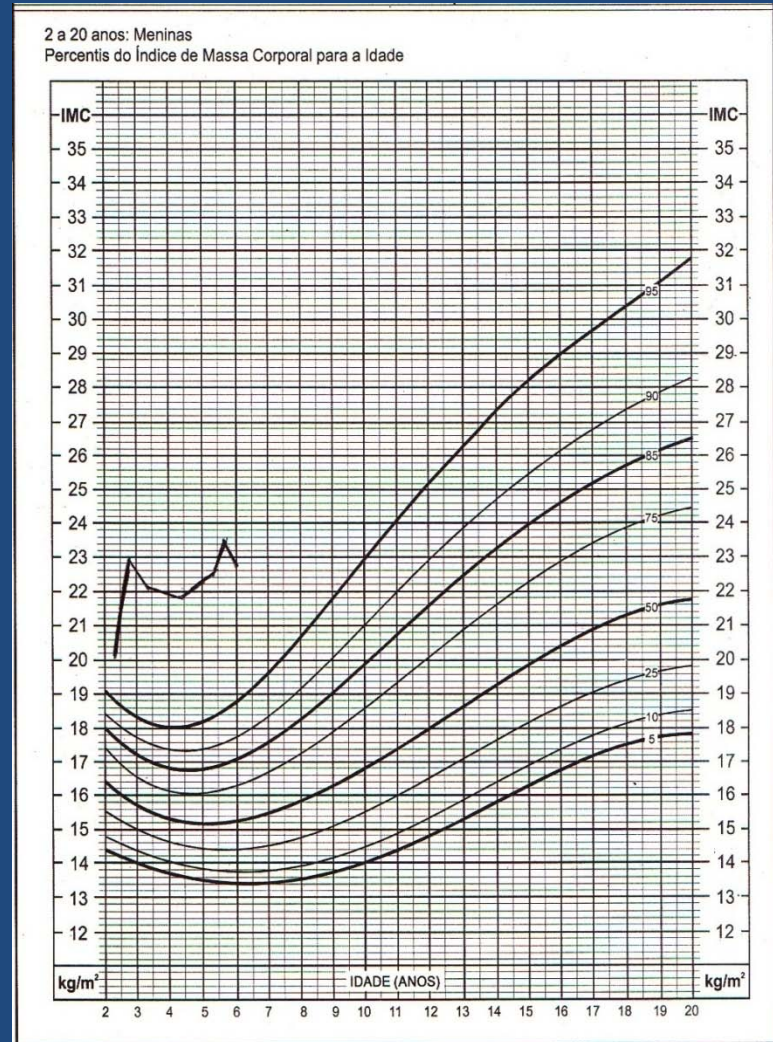
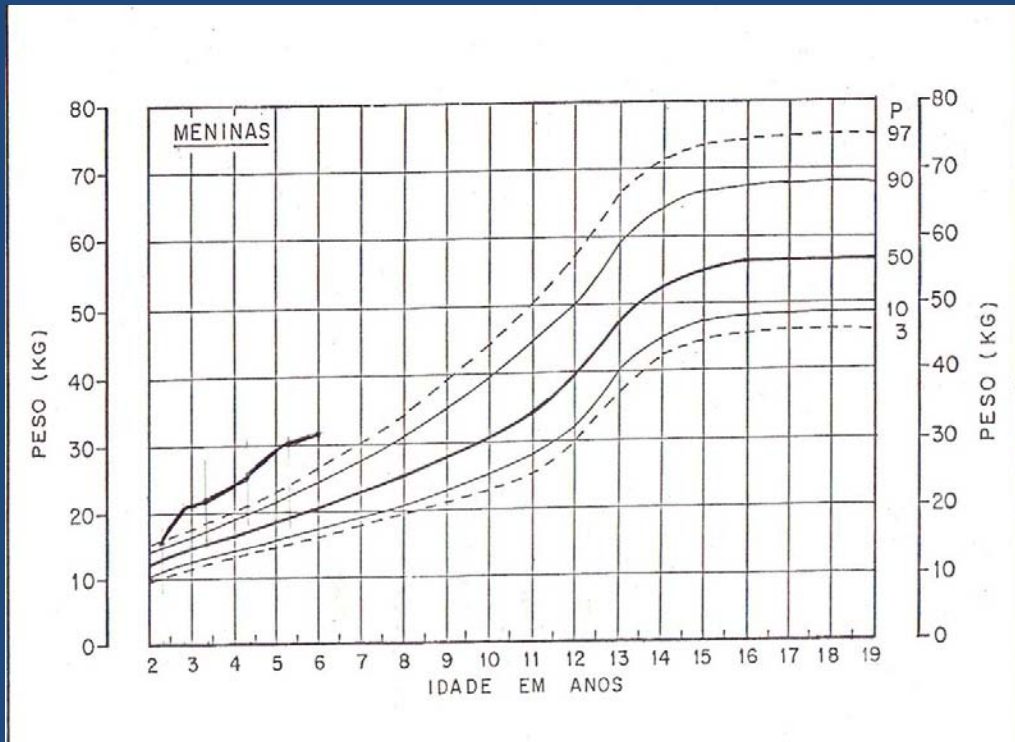
**Síndrome
Metabólico**

Catch-up



↑ significativo de la velocidad de crecimiento mayor al esperado para la edad y sexo, luego de una fase de desaceleración o detención

Crecimiento de una niña nacida prematura



DOHaD

Origen del Desarrollo de la Salud y la Enfermedad

Nueva área de conocimiento biomédico relacionada a la determinación de nuevas *fuentes de causalidad* entre eventos ocurridas en fases precoces del desarrollo y el **surgimiento de Enfermedades Crónicas** a lo largo del ciclo vital.

DOHaD

Esclarecer la influencia de eventos adversos ocurridos en fases precoces del desarrollo humano sobre el patrón de salud y enfermedad a lo largo de la vida

Modelos de causalidad

- Teoría del *fenotipo ahorrador*
- Programación
- Respuestas adaptativas predictivas
- Concepto de *concordancia o contraste*



Developmental origins of health and disease (DOHaD)

Patrícia P. Silveira,¹ André K. Portella,² Marcelo Z. Goldani,³ Marco A. Barbieri⁴

Abstract

Objective: To present a new branch of scientific knowledge, known as the developmental origins of health and disease (DOHaD), covering its concepts, study methods and ethical considerations in addition to the prospects for this area of knowledge.

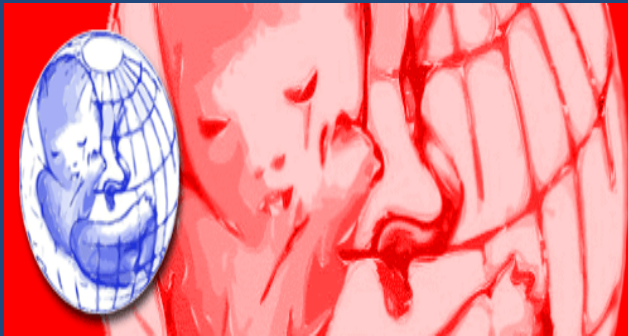
Sources: A non-systematic review of the biomedical literature intended to identify historical and current references related to the subject under discussion.

Summary of the findings: Recent studies demonstrate associations between aggressions suffered during the initial phases of somatic development and amplified risk of chronic diseases throughout life, such as obesity, diabetes and cardiovascular diseases. A variety of models have been proposed in attempts to better explain these associations, such as the thrifty phenotype, programming and predictive adaptive response theories and the concept of match or mismatch. Some of the mechanisms possibly involved in these processes are: effects of the environment on gene expression, through epigenetic mechanisms; effects of hormonal signals transmitted to the fetus via the placenta or the newborn via lactation.

Conclusions: DOHaD draws together information originating from many different areas of knowledge, proposing new investigative methodologies to elucidate the influence of adverse events that occur during early phases of human development on the pattern of health and disease throughout life. This new scientific field proposes new models of causality and of the mechanisms involved in the emergence and development of chronic diseases. The results of these investigations may result in a significant impact on the prevention of chronic diseases, and also on health promotion in different phases of life.

J Pediatr (Rio J). 2007;83(6):494-504: DOHaD, programming, Barker hypothesis.

Mecanismos: efecto del medio ambiente sobre la expresión génica, a través de mecanismos epigenéticos; efecto de señales hormonales transmitidas al feto vía la placenta o al niño vía la lactancia



DOHaD

International Society
for Developmental
Origins of Health
and Disease



DOHaD 2015

8th -11th November 2015

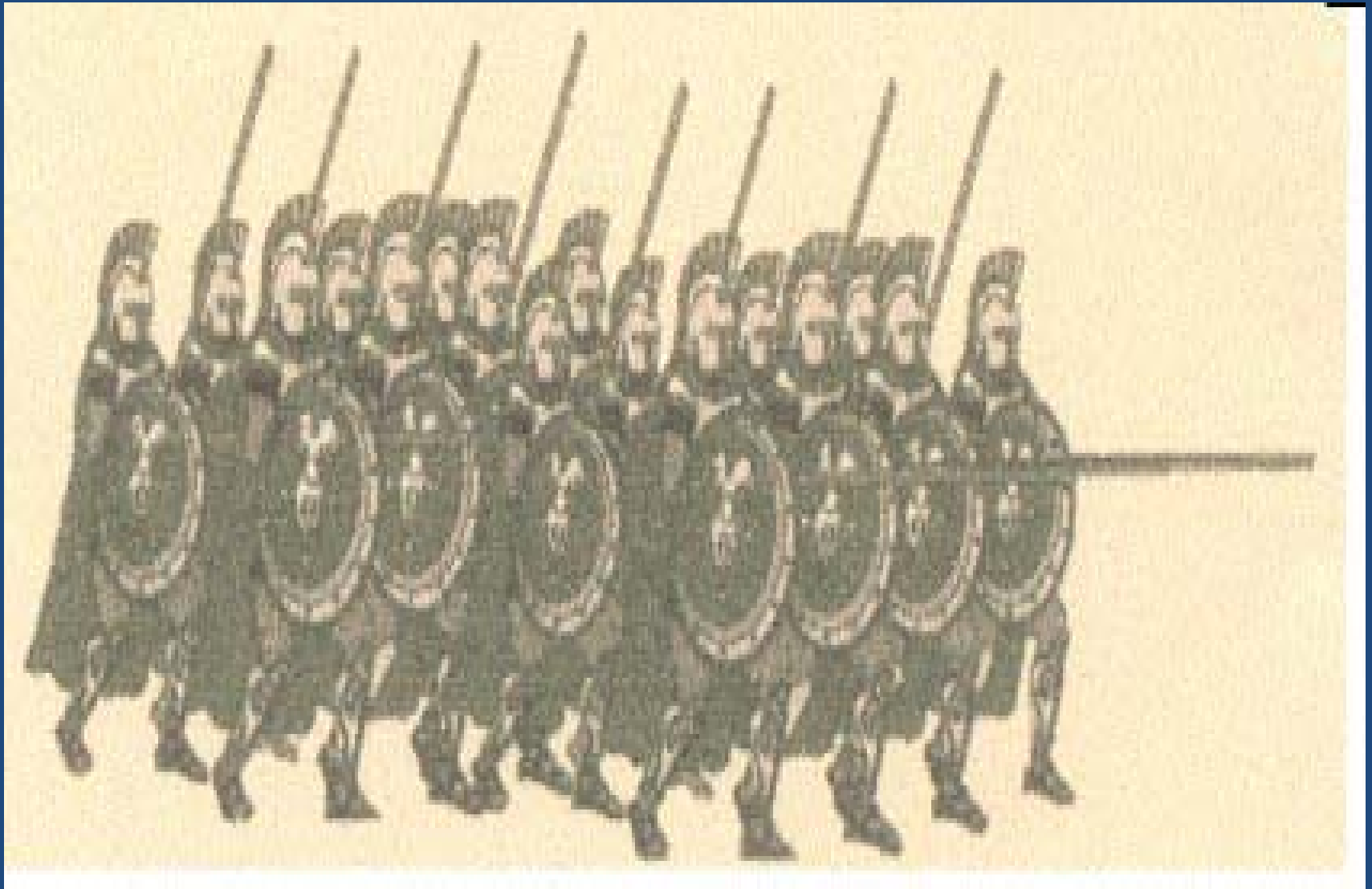
Cape Town International Convention Centre,
Cape Town, South Africa

9th WORLD CONGRESS
**DEVELOPMENTAL ORIGINS
OF HEALTH AND DISEASE**



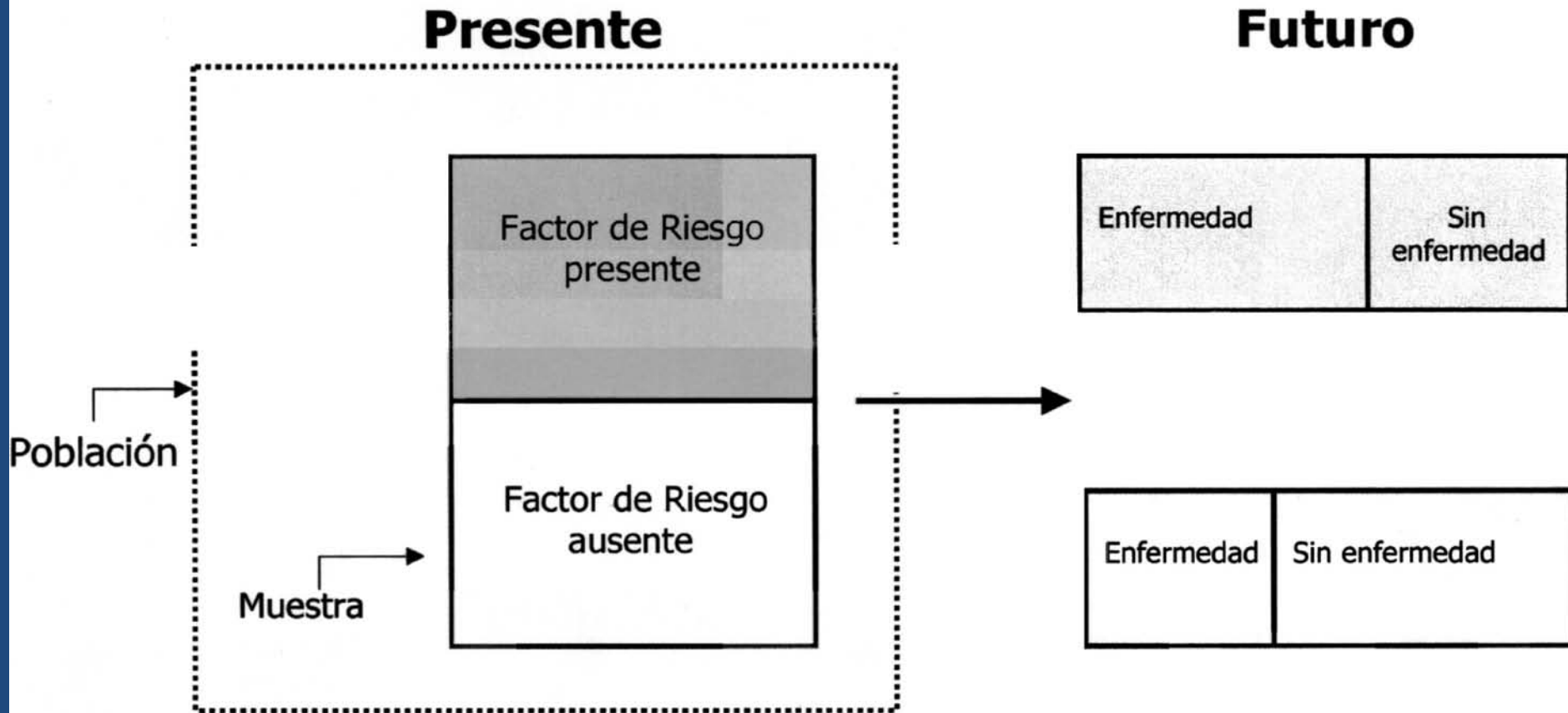
Modelos de Investigación DOHaD





Cuerpo de infantería del ejército de la antigua Roma, compuesto por varias centurias.

Diseño de Cohorte



Pasos:

1. Seleccione una muestra de la población
2. Mida las variables predictoras (factor de riesgo presente o ausente)
3. Siga la cohorte
4. Mida la variable resultado (enfermedad presente o ausente)

Algunos resultados de los
estudios sobre DOHaD de las
cohortes de Ribeirão Preto,
São Paulo, Brasil

(38 entre 2009-2015, o sea

5 publicaciones por año)

Perfil Epidemiológico Perinatal en 3 cohortes al nacimiento de Ribeirão Preto, SP, Brazil

Cohortes de Ribeirão Preto	1978/79	1994	2010
Prematuridad	7.6%	12.6%	14.5%
Bajo peso al nacer	7.2%	10.6%	9.4%
Mortalidad Fetal	22.4‰	9.5‰	5.7‰
Mortalidad Neonatal	23.3‰	10.9‰	5.9‰
Mortalidad Infantil	36.4‰	16.9‰	8.6‰
Cesárea	30.3%	50.8%	58.6%
Média de peso al nacer	3236g	3113g	3131g

Machado Arruda SP, da Silva AA, Kac G, Vilela AA, Goldani M, Bettiol H, Barbieri MA. **Dietary patterns are associated with excess weight and abdominal obesity** in a cohort of young Brazilian adults. Eur J Nutr 2015 Aug 29.

Bernardi JR, Pinheiro TV, Mueller NT, Goldani HA, Gutierrez MR, Bettiol H, Moura da Silva AA, Barbieri MA, Goldani MZ. **Cesarean delivery and metabolic risk factors in young adults: a Brazilian birth cohort study.** Am J Clin Nutr. 2015;102(2):295-301.

de Melo AS, Dias SV, Cavalli Rde C, Cardoso VC, Bettiol H, Barbieri MA, Ferriani RA, Vieira CS. **Pathogenesis of polycystic ovary syndrome: multifactorial assessment from the foetal stage to menopause.** Reproduction. 2015 ; 150(1):R11-24.

Ribeiro MR, de Brito e Alves MT, Batista RF, Ribeiro CC, Schraiber LB, Barbieri MA, Bettiol H, da Silva AA. **Confirmatory factor analysis of the WHO Violence Against Women instrument in pregnant women: results from the BRISA prenatal cohort.** PLoS One 2014; 9 (12):e115382.

Cardoso VC, Meritano J, Silva AA, Bettiol H, Barbieri MA, Grandi C. **Size at birth and blood pressure in young adults: findings from a Brazilian birth cohort study.** Rev Saude Publica 2012 ;46(6):978-87.

Do intrauterine growth restriction and overweight at primary school age increase the risk of elevated body mass index in young adults?

H. Bettioli¹,
D. Sabbag Filho²,
L.S.B. Haeffner³,
M.A. Barbieri¹,
A.A.M. Silva⁴,
A. Portela⁵,
P. Silveira⁵
and M.Z. Goldani⁵

¹Departamento de Puericultura e Pediatria, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brasil

²Faculdade de Medicina de Marília, Marília, SP, Brasil

³Departamento de Pediatria e Puericultura, Centro de Ciências da Saúde, Curso de Medicina, Universidade Federal de Santa Maria, Santa Maria, RS, Brasil

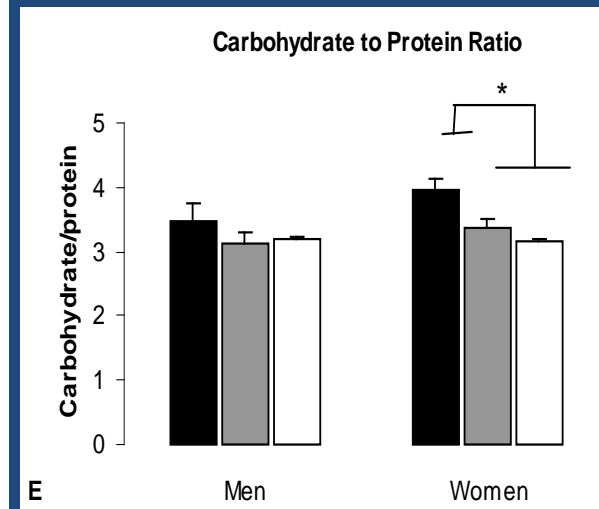
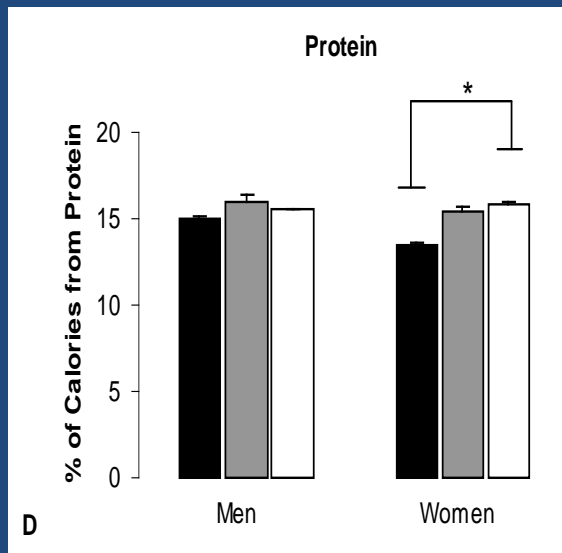
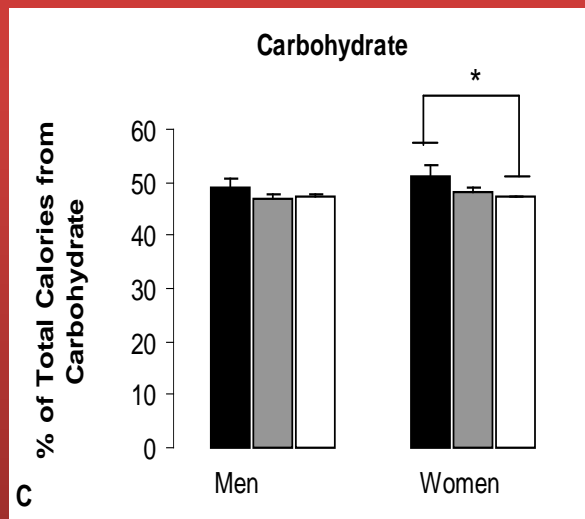
⁴Departamento de Saúde Pública, Universidade Federal do Maranhão, São Luís, MA, Brasil

⁵Departamento de Pediatria e Puericultura, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil

Severe Intrauterine Growth Restriction is Associated With Higher Spontaneous Carbohydrate Intake in Young Women

MARCO A. BARBIERI, ANDRÉ K. PORTELLA, PATRÍCIA P. SILVEIRA, HELOÍSA BETTIOL, MARILYN AGRANONIK, ANTÔNIO A. SILVA, AND MARCELO Z. GOLDANI

Department of Child Care and Pediatrics [M.A.B., H.B.], Faculty of Medicine of Ribeirão Preto, São Paulo 14040-904, Brazil; Department of Pediatrics [A.K.P., P.P.S., M.A., M.Z.G.], UFRGS, Rio Grande do Sul 90035-003, Brazil; Department of Public Health [A.A.S.], Federal University of Maranhão, São Luis, Maranhão 65020-070, Brazil



Macronutrients consumption in severely restricted (Sev_R), moderately restricted (Mod_R) and non restricted (No_GR) individuals. C: Percentage of the total calories derived from carbohydrate; D: Percentage of the total calories derived from protein; E: Carbohydrate to protein ratio. *Two-way ANOVA followed by LSD with interaction evaluation, $p < 0.05$.



Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study¹⁻³

Helena AS Goldani, Heloisa Bettiol, Marco A Barbieri, Antonio AM Silva, Marilyn Agranonik, Mauro B Morais, and Marcelo Z Goldani

¹ From the Department of Pediatrics, Hospital de Clínicas de Porto Alegre, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil (HASG, MA, and MZG); the Department of Pediatrics, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil (HB and MAB); the Department of Public Health, Faculdade de Medicina, Universidade Federal do Maranhão, Brazil (AAMS); and the Department of Pediatrics, Faculdade de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil (MBM).

Alcohol consumption during pregnancy and perinatal results: a cohort study

Consumo de álcool durante a gravidez e resultados perinatais: um estudo de coorte

Mariana Sbrana^I, Carlos Grandi^{II}, Murilo Brazan^I, Natacha Junquera^I, Marina Stevaux Nascimento^I, Marco Antonio Barbieri^{III}, Heloisa Bettiol^{IV}, Viviane Cunha Cardoso^V

Ribeirão Preto Medical School, Universidade de São Paulo (USP), Ribeirão Preto, São Paulo, Brazil

Sao Paulo Med Journ 2016

Estudios de Cohorte

- La Mayoría son realizados en países desarrollados
 - Donde ocurre la < parte de los nacimientos
 - Diferencias sociales pequeñas
- Epidemiología → exposición y factores de confusión
- Transición epidemiológica



STUDY PROTOCOL

Open Access

A protocol to identify non-classical risk factors for preterm births: the Brazilian Ribeirão Preto and São Luís prenatal cohort (BRISA)

Antônio Augusto Moura da Silva^{1*}, Vanda Maria Ferreira Simões¹, Marco Antonio Barbieri², Viviane Cunha Cardoso², Claudia Maria Coelho Alves¹, Erika Bárbara Abreu Fonseca Thomaz¹, Rejane Christine de Sousa Queiroz¹, Ricardo Carvalho Cavalli², Rosângela Fernandes Lucena Batista¹ and Heloísa Bettiol²

RIBEIRÃO PRETO BIRTH COHORT 2010: METHODOLOGY AND MAIN FINDINGS

Cardoso V, Grandi C, Vitti F, Kobori S, Furlan R, Rodrigues I, Ressel L, Gutierrez M, Cavalli R, Bettiol H, Barbieri M

Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (FMRP-USP), Brasil

Objectives: To describe the study methodology of a 2010 population birth cohort in Ribeirão Preto, and present the main findings.

Methods: 7704 mothers and their 7799 newborns were evaluated in 8 maternities in Ribeirão Preto, in 2010. The study included all mothers who delivered at Ribeirão Preto hospitals and agreed to participate. Data were collected from surveys and medical records, after childbirth.

Results: The average maternal age was 27 years old (SD=6.2) and 9.8 years of education (SD=2.3), whereas 76.6% had 9 or more years of education. 13.7% of mothers had no partner, and 1.4% did not receive prenatal care. 12.6% had hypertension and 6% had gestational diabetes. 22.8% of mothers consumed alcoholic beverages, 11.8% smoked and 66.8% consumed coffee during pregnancy. 12.6% were obese and 24.2% overweight. The mean gestational age was 270 days (SD=18.1). The rate of cesarean was 58.6% and 0.6% had stillbirth. 7799 children were born, being 92 twins and 3 triplets. The mean of birth weight was 3119 grams (SD=574): 10% low birth weight, 25% underweight and 4% high weight. 15% of the newborn were preterm and 1.2% had congenital defect.

Conclusions: Mothers of this cohort showed a high level of education and overweight/obesity. Prenatal care rate was wide and there was high frequency of premature newborns and cesarean



COORTES - RIBEIRÃO PRETO

Pesquisando da gestação até sempre

<http://coortes.fmrp.usp.br/#>

Início

Contato

Coortes

Histórico

NESCA na imprensa

Pesquisadores

Publicações



1978



1994

1979



Coortes 78/79

A mais antiga coorte brasileira de nascimentos teve início em junho de 1978 e todas as mães residentes no município foram entrevistadas nos oito hospitais-maternidade...

[Leia mais ▶](#)

Horário e informações





Epidemiologia Ufpel agregó una foto nueva.

23 de diciembre de 2015 · 🌐

Facebook

Coorte 2015 1º aninho

Em 2016, as crianças da Coorte 2015 completam o 1º ano de vida. É o momento de realizarmos nova etapa de acompanhamento da saúde dos participantes. Pouco antes do aniversário, a equipe da Coorte vai entrar em contato com as mães para agendar a visita.

Feliz (1º) ano novo!



COORTE 2015
1º aninho

CH



¿Y por casa cómo andamos?

- Mientras Brasil, Chile y Uruguay lideran la investigación de DOHaD en Latinoamérica **DESDE HACE 35 AÑOS....**
- Argentina la ignora **TOTALMENTE !!**
- Es tiempo que nos unamos para saber cómo les va a nuestros niños en el curso de sus vidas.

Los primeros 1000 días,
de la concepción hasta los 24
meses

1,000 DAYS

"We believe fervently that improving nutrition for pregnant women and children under two is one of the smartest investments we or anyone can make."

— September 20, 2011

Learn More >>>

>> GET UPDATES ABOUT 1,000 DAYS

enter email address

TAKE ACTION: Horn of Africa Crisis



What's at Stake?

Over 100 days after declaring famine, more than 13 million people throughout the Horn of Africa continue to face a devastating combination of drought, food crisis and conflict. The most vulnerable - infants, young children, pregnant women and new mothers - remain in danger of

THE 1,000 DAYS BLOG

MORE →



Thousand
Days

A sight-and life-saving root
12.13.2011

Vitamin A deficiency affects an estimated 140 million children in Africa and Southeast Asia. That's 140 million children that are...

READ MORE →

- Los **estudios epidemiológicos** en diferentes partes del mundo relacionan la influencia de determinados **factores ambientales** al inicio de la vida con alteraciones en la expresión de la **carga genética** del individuo, determinando un **patrón de salud-enfermedad** peculiar.
- Igualmente, **estudios clínicos** apuntan en la misma dirección, sugiriendo una fuerte asociación entre **exposiciones ambientales** ocurridas en la vida fetal o en las fases iniciales de la vida extra-uterina y el surgimiento de enfermedades crónicas a lo largo de la vida.

Ventana de Oportunidades

Dilema del crecimiento rápido

¿Que hacer y cuáles son las consecuencias del crecimiento rápido en niños pequeños?

Crecimiento rápido

≠

Catch-up (crecimiento compensador)

Capital Humano

Concepto

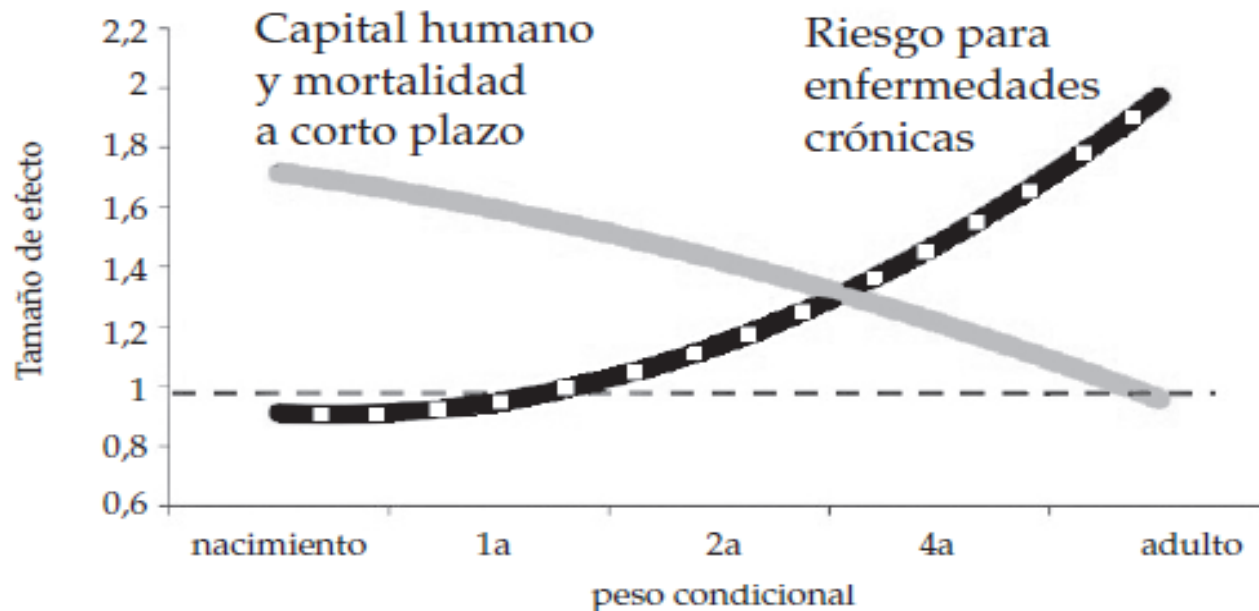
Falta de inteligencia, escolaridad, altura, fuerza muscular, capacidad de gestar hijos saludables en la próxima generación.

Preocupación

Ganancia de peso puede ser muy buena para indicadores como escolaridad y capital humano, pero existe mayor riesgo de ECNT.

Momento de la Ganancia de Peso

FIGURA 6. *Ganancia de peso precoz en países de ingresos bajos*





¡¡ Muchas gracias !!