Our Physical & Mental Health Are Powered By Three Concepts

Youth Motivation
Mid-Life Life Style
Aging Heart-Mind
# A Transition From Disease to Health – 2010-2020
## Cardiovascular & Mental

<table>
<thead>
<tr>
<th>Step</th>
<th>Transition</th>
<th>Disease</th>
<th>Condition</th>
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<tr>
<td>1</td>
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<td>CAD</td>
<td>CVD</td>
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<td>Subclinical</td>
<td>HRP</td>
<td>DBD</td>
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<tr>
<td>2</td>
<td>Health</td>
<td>IOM</td>
<td>SHE</td>
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**Abbreviations:**
- **CAD** – Coronary Artery Disease
- **CVD** – Cerebro Vascular Disease
- **HRP** – High Risk Plaque
- **DBD** – Degenerative Brain Disease
- **IOM** – Institute of Medicine
- **SHE** – Science Health & Education
ANGINA, MYOCARDIAL INFARCTION

C=Clinical
B=Basic

C) COMPLEX CORONARY ARTERY DISEASE
C) CORONARY INTERVENTION

C) MT - CARDIOVASCULAR RISK FACTORS (7)

>2RF = MI-Stroke
25% in 10 Yrs
75% in 30 Yrs

### C) Complex Coronary Artery Disease

**Evidence Base Management - $ 250 Million**

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>MVD</th>
<th>DM</th>
<th>INTERV. MT.</th>
<th>EP.</th>
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<td>-</td>
<td>++</td>
<td>-</td>
<td>Revasc &lt;CABG&lt;br&gt;Sx Sc. (Reg) &lt;CABG&lt;br&gt;DM – Int.SxSc. &lt;CABG&lt;br&gt;(Ischemic Score)</td>
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<td>INTERV. vs RX = EP&lt;br&gt;Sx Sc &lt;CABG, Revasc. Xover 42%&lt;br&gt;(ischemic Score?)</td>
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<td><strong>FREEDOM</strong></td>
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<td>++</td>
<td>+</td>
<td>Largest DB DM&lt;br&gt;FREEDOM Score (3)&lt;br&gt;Rx Approach-Polypill&lt;br&gt;Non Invasive Imaging</td>
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</table>

- **TRIAL** indicates different clinical trials.
- **MVD**, **DM**, **INTERV. MT.**, and **EP.** represent different variables or categories.
- **Data** section provides additional details about the outcomes and comparisons.
B). Imaging the Atherothrombotic Process

HIGH RISK PLAQUE - < ACTIVE INFL.

Embryonic Stem Cell Derived, CV Progenitor Cells (FLK Positive Cells)

E Adler, ZA Fayad, S Kattman, G Keller et al 2010 (Subm)
Senescence-Associated Telomere Changes

1. INTRINSIC: Telomere-dependent, “relicative senescence”
   - Replicative senescence
   - Short telomeres
   - p5 → p21^{Clp1/WAF1}
   - “p16/Rb pathway”
   - Cellular senescence
   - Human cells

2. EXTRINSIC: Telomere-independent, “STASIS”
   - Stress → p16^{INK4a}
   - CDK4/6 → p-Rb
   - STATIS

Oxidative Stress - Aging, Cancer
Smoking ?, Low Caloric diet ?, Exercise ?,
**HIGH RISK PLAQUE -> ACTIVE INFL.**

Ph.1
PGC

Ph.2
VAS. V.

Ph.3
HDL

LDL

CAMs

TF

MMPs

Extracellular Matrix

Fibroblasts

Vasa Vasorum


PDGF

ET

SMC contraction
migration
proliferation

TF

ET
Dynamic Contrast Enhanced (DCE) MRI (Gd)

Pre-contrast | Post-contrast 2 min | Post-contrast 8 min

T1W

Pre-contrast | Post-contrast

LC = lipid rich/necrotic core
FC = Fibrous cap

Kerwin et al. MRM 59; 507, 2008
Coronary FDG Uptake

CT Angiogram

Fused PET and CTA Images

JH Rudd, V Fuster, ZA Fayad et al. JACC 2011 (In Press) – PET, Ao-Ca-Cor
HIGH RISK PLAQUE - APOPTOSIS

THROMBUS

Ph.1
PGC

Ph.2
VAS. V.

Ph.3
HDL

LDL

CAMS

TF
MMPs

Extracellular Matrix
Fibroblasts
Vasa Vasorum

SMC contraction
migration
proliferation

3) Reduction in gene & Protein Tissue Factor Expression
1) Badimon JJ, Badimon L, Fuster V, JCI 1990; 85:1234 –Apo A1 Rabbits
2) Nissen SE JAMA 2003; 290:2292 – Apo A1 in Humans - IVUS
CETP Inhibition (Anacetrapib)
Changes in Cholesterol Levels

DEFInE Investigators (CP Cannon et. al.) *N Engl J Med* 2010, Nov 17
A Transition From Disease to Health – 2010-2020
Cardiovascular & Mental

1
Complex
2
From CAD to CVD
From HRP to DBD
From IOM to SHE

CAD – Coronary Artery Disease
HRP - High Risk Plaque
IOM – Institute of Medicine
CVD – Cerebro Vascular Disease
DBD – Degenerative Brain Disease
SHE – Science Health & Education
C) Cardiovascular (Cerebrovascular)

HEART MI

Thrombi

Occlusion of anterior interventricular branch of

1) Emboli
2) Thrombi
3) Hemorrh

BRAIN - STROKE

Cardiovascular & Mental Health
C) SYMPTOMATIC CAROTID ENDARTER. VS STENTING – $200 Million

### All-cause death

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<th>CAS n/N</th>
<th>CEA n/N</th>
<th>RR (95% CI)</th>
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Overall effect: p=0.04 (heterogeneity: p=0.61, r=0%)

### Any stroke or death

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<th>RR (95% CI)</th>
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<tr>
<td>CREST</td>
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<td>1.86 (1.20-2.90)</td>
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Overall effect: p<0.0001 (heterogeneity: p=0.19, r=37.1)

P Amarenco et al., Lancet 2010; 376:1028 - CEA,Complexity, - CAS,Morbidity
B) Integration of Noninvasive Imaging PET/MRI for Early Identification of CVD
<table>
<thead>
<tr>
<th>Transition From Disease to Health – 2010-2020</th>
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<tbody>
<tr>
<td>Cardiovascular &amp; Mental</td>
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<table>
<thead>
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**Abbreviations**

- CAD – Coronary Artery Disease
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- SHE – Science Health & Education
PESA
40-54y, n= 4,000 , FU 0,3,6 y

Life Style ?

Omics – Copenhagen Heart Study, Framingham,
HRP - BioImage Study – Mobile Units

PI: Valentin Fuster, Co-PI: Erling Falk, Peter Muntendam - AHJ 2010;160:49
Both conventional longitudinal scan and transverse (axial) sweep of carotids:

- “Manual 3D”: T.P Area
- 3D transducer: P Volume

37% of subjects with plaques would have been missed in conventional longitudinal scans

Plaque Definition: focal structure encroaching into the arterial lumen of at least 0.50 mm or 50% of surrounding IMT value
Events 8 mo: 94 – 34 Heart Attacks -
1) Extensive Plaque Burden - 2) Bilateral Predictive (X2 FRS)
3) No Change in Life Style? - 4) Economic?

H Sillesen, V Fuster, E Falk, C McCall, P Muntendam AHA 2011
PESA
40-54y, n=4,000 FU 0,3,6 y

Life Style ?

HRP > 55y,
N=7000 FU 3y

Predictive ?

“Omics – Copenhagen Heart Study, Framingham,”
A Transition From Disease to Health – 2010-2020
Cardiovascular & Mental

1
Complex -- From CAD to CVD

2
Subclinical -- From HRP to DBD

Health -- From IOM to SHE

CAD – Coronary Artery Disease
HRP – High Risk Plaque
IOM – Institute of Medicine

CVD – Cerebro Vascular Disease
DBD – Degenerative Brain Disease
SHE – Science Health & Education
ADVANCED AGE, HYPERTENSION AND DEMENTIA
SBP AND SHORT PORTABLE MMSE SCORE
BY INCREASING AGE GROUPS

Mean systolic blood pressure (mmHg)

HW Querfurth, FM LaFerla. NEJM 2010; 362:329 - Imaging
High Resolution 8-T Gradient Gd-Enhanced Echography Slices

Mechanisms of Disease: Alzheimer’s Disease

1. C. Iadecola et. al. Stroke 2009;40[suppl 1]:S40.
2. HW Querfurth, FM LaFerla. NEJM 2010; 362:329
   Ischemia affects 60 to 90% of patients with Alzheimer’s
3. Mount Sinai Journal of Medicine 2010; 77:82-102
   Hypertension, Hypotension, Cholesterol, Diabetes, Smoking
A Transition From Disease to Health – 2010-2020
Cardiovascular & Mental

1
Complex

2
From CAD to CVD

Subclinical

From HRP to DBD

Health

From IOM to SHE

CAD – Coronary Artery Disease
HRP - High Risk Plaque
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CVD – Cerebro Vascular Disease
DBD – Degenerative Brain Disease
SHE – Science Health & Education
Promoting Cardiovascular Health

National Heart, Lung, and Blood Institute

Institute of Medicine, of The National Academy of Sciences

Report Brief, Report Summary, and Full Prepublication Report can be downloaded for free: www.iom.edu/globalcvd

Chair – Valentin Fuster
Projecting Deaths by Cause, 2004, 2015, 2030

K2 - Prevalence of CVD is Increasing
Treatment (Live Longer) and Technology ($)

Rx, H-I $368 Bill, X3 10y
Rx, L-I MI, Pocket 80%
Rx, H-I $ 95% - Prev $ 5%

K3

**POLICY APPROACHES**
(Global; National; Local)

- Financial
- Legal
- Regulatory
- Trade

**Environment To Enable Individuals To Make and Maintain Healthy Choices**

**INDIVIDUAL**

**FAMILY**

**NEIGHBORHOOD, COMMUNITY**

**Enhancement of Knowledge, Motivation, and Skills of Individuals**

**HEALTH COMMUNICATION**

**HEALTH CARE DELIVERY**

**DETERMINANTS**

- Globalization
- Demographic Change
- Social Determinants
- Health Inequities
- Education
- Cultural and Social Norms
- Biological Risk
- Behavioral Risk

**WIDER SOCIETY**

- Preventive, Diagnostic, Therapeutic, Rehabilitative Services
- Health Workforce
- Drugs & Technologies
- Systems Infrastructure
- Quality of Care
- Access to Care
A1 - WE KNOW THE RISK FRS CONTRIBUTING TO CVD

IT SEEMS SIMPLE...

Consumption
- Foods/
  - Calories
- Fats/oils
- Salt
- Tobacco

Activity
- Work
- School
- Leisure

Blood pressure
- Cholesterol
- Obesity
- Blood glucose

Incidence

Morbidity

Mortality

RELUCTANT TO ACCEPT
NO ADHERENCE
## A2 - Sharing for Action: Essential Functions

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# A3 - Transition From Disease to Health – 2010-2020

## Cardiovascular & Mental Complexes

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<td>1</td>
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### Abbreviations
- **CAD**: Coronary Artery Disease
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- **DBD**: Degenerative Brain Disease
- **IOM**: Institute of Medicine
- **SHE**: Science Health & Education
SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street
B. Adults Cultural Groups - GHP
C. Adults Regulations & Law – NY
D. Millenium Project – Infrastructure
E. Polypill – Adherence & Economy
F. Youth – It is Never too Early
A1 - The Early Relationship Between Parent, Child & Environment are Crucial to Later Development

Many adolescents do not get enough exercise, more than half watch too much TV, and most consume less than the recommended amount of fruits and vegetables.

A. Bogota (n=6000), Madrid, Cardona (n=1200) Health, Drugs, Tolerance

Randomized Study: End Points 1 Year – 20 Years
IMPACT OF THE HEALTHY HABITS INTERVENTION IN USAQUEN

Changes in knowledge, attitudes and habits in Children

Changes in knowledge, attitudes and habits in Parents

Changes in knowledge, attitudes and habits in Teachers

Baseline | Final
--------|--------
| | Intervention | Control

Baseline | Final
--------|--------
| | Intervention | Control

Baseline | Final
--------|--------
| | Intervention | Control
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**Project Expansion Through Partners**
SHE - 20 Schools in Madrid and Cataluña

International Foundation for Science, Health and Education (SHE)

Educative Goal: Healthy Habits for Children between 3 and 16 Years

- Acquisition of Healthy Food Habits
- Physical Activity
- Knowledge of How Your Body and Heart Works
- Acquisition of Preventive Habits to Avoid Addictions

Sí!
Programa de Salud Integral
SHE – Progress & Dissemination

International Foundation for Science, Health and Education (SHE)

EDUCATIONAL BOOKS

CHILDREN

3-6
Valentín Fuster
Monstruos supersanos

5-8
Valentín Fuster
La Mediana
Ciencia de la
Salud

9-14
Valentín Fuster
Pequeña Ciencia
de la Salud

GENERAL PUBLIC

Ferran Achúria
Valentín Fuster
Josep Corbella

LA COCINA DE LA SALUD

VALENTÍN FUSTER
JOSE LUIS SAMPEDRO
LA CIENCIA Y LA VIDA

VALENTÍN FUSTER
Luis Torres Marín
CORAZÓN Y MENTE

Si!
Programa de Salud Integral
SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street

B. Adults Cultural Groups – GHP

C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

F. Youth – It is Never too Early
B. GHP – Background (LMIC) and Observational Objectives

1975

2000
Risk Factors:

- Overweight or Obese
- Hypertension
- Diabetes
- Cholesterol
- Smoking

RISK FACTORS: MAN

RISK FACTORS: WOMAN
1) GHP INCENTIVE GROUP APPROACHES

- Blood Pressure
- Physical Activity
- Weight / Diet
V Fuster, R Vedanthan, BB Kelly, Circ 2011 (In Press)
SHE - Global Demonstration Projects

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D. Millenium Project – Infrastructure
E. Polypill – Adherence & Economy
F. Youth – It is Never too Early
C. The Epidemic of CVD & The Law

Hypertension?
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E. Polypill – Adherence & Economy

F. Youth – It is Never too Early
D. Africa’s Ecological Zones & Initial 12 MV Sites
UN & Earth Institute, NY

V Fuster, S Sachs, R Vedanthan R. NHLBI / Rwanda Project, 2010
SHE - Global Demonstration Projects

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F. Youth – It is Never too Early

Sustainability
Number of patients /healthy volunteers included: 368
A. Children (3-8yrs) – Sesame Street
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C. Adults Regulations & Law – NY
D. Millenium Project – Infrastructure
E. Polypill – Adherence & Economy
F. Youth – It is Never too Early
SPANISH YOUTH 2010
Survey by Foundation SM
3513 young Ages 15-24 y

HEALTH IN SPAIN 2010
European Survey (EES09)
22188 over age 16 y

ALCOHOL & DRUGS IN SPAIN 2010
House Survey (EDADES)
Large population over Age 16 y

INNOVATION AND BUSINESS 2010
Survey by McKinsey’s
50 Business People
1. Low in Confidence 65%
2. Low in Future Pesimistic 62%
3. Low in Education 4.5% PIB
F1. The Future of Well Being Promotion of Mental Health

- Time to Reflect Calmer (Stress)
- Talent to Discover Fulfilled (Neurosis)
- Transmit Positive Happiness (Hostage)
- Tutoring the Young Responsible (Future)
SPANISH YOUTH 2011

1. LOW IN CONFIDENCE 65%

2. LOW IN FUTURE Pesimistic 62%

3. LOW IN EDUCATION 4.5% PIB
F2. Lifetime Happiness

1. “Happiness comes from our own attitude. If your mental attitude is correct, even in a hostile atmosphere, you feel happy.” (Dalai Lama)

2. “Success is getting what you want. Happiness is accepting what you get.” (Dale Carnegie)

3. “Happiness is the key to success. If you love what you are doing, you will be successful”. (Albert Schweitzer)

4. “Happiness is when what you think, you say, and you do are in harmony”. (M. Gandhi)

5. “Happiness for a lifetime – help someone else”
1. LOW IN CONFIDENCE 65%

2. LOW IN FUTURE Pesimistic 62%

3. LOW IN EDUCATION 4.5% PIB

SPANISH YOUTH 2011
F3. Pro CNIC Board of Trustee
Funding – 38%

1.- César Alierta
Telefónica
2.- Ignacio Polanco
Grupo Prisa
3.- Emilio Botín
Fundación Marcelino Botín
4.- José Manuel Entrecanales
Acciona, Pro CNIC F. Pres.
5.- Valentín Fuster
CNIC Scientific President
6.- Isidro Fainé
La Caixa
7.- Francisco González
BBVA
8.- Luis Suárez de Lezo
Repsol YPF
9.- Ignacio Garralda
F. I. Médica Mutua Madrileña
10.- Carlos Martínez Echevarría
Fundación Ramón Areces
11.- Salvador Gabarró
Gas Natural
12.- Luis de Carlos
Uría Menéndez
13.- Rodolfo Martín Villa
Fundación Endesa
14.- Miquel Roca
Fundación Abertis
15.- Pablo Isla
Inditex

Intramural Education (12)
Extramural Grants (2- 4 x year)
Equipment (Imaging etc)

SCIENCE July 8, 2005 & Sept 1, 2006
THE LANCET Aug 19, 2006
F3. CNIC (Spain) - Discovering / Tutoring

A Transition From Disease to Health – 2010-2020
Cardiovascular & Mental

1. Complex
   -- From CAD to CVD

2. Subclinical
   -- From HRP to DBD

Health
   -- From IOM to SHE

HRP – High Risk Plaque  
IOM – Institute of Medicine

CVD – Cerebro Vascular Disease  
DBD – Degenerative Brain Disease  
SHE – Science Health & Education
Our Physical & Mental Health Are Powered By Three Concepts

Youth Motivation
Mid-Life Life Style
Aging Heart-Mind