Personalized Preventive Care for Cancer

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- Evidence of personalized preventive research on cancer
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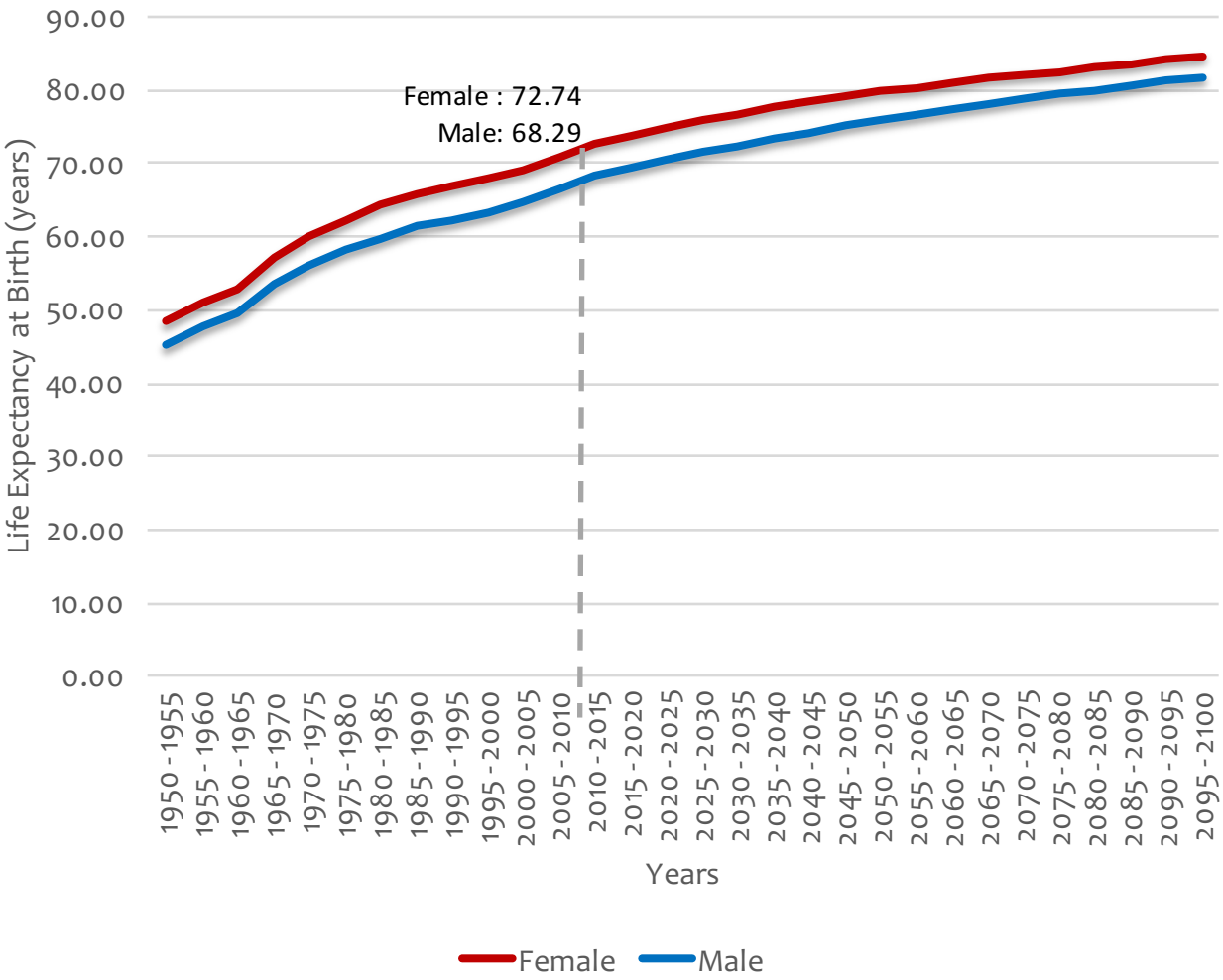
  - Current interests on cancer
- Preparation for future needs
  - Collaboration is key
  - The next cohort for cancer in epidemiology

Part I.

Increased importance of personalized preventive care

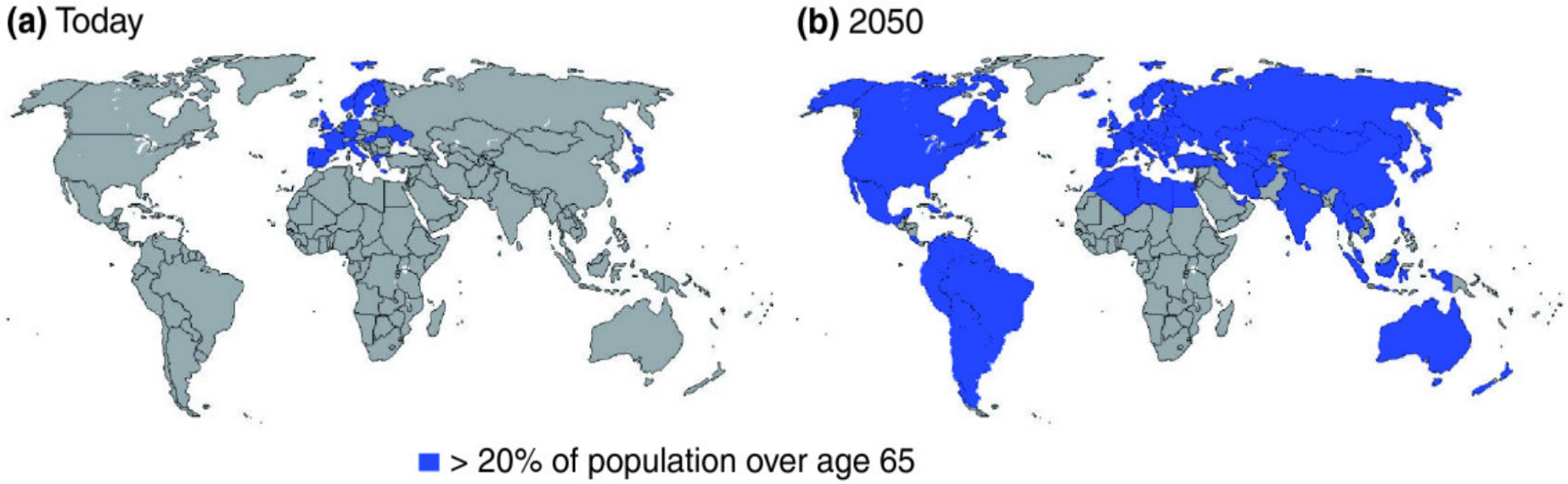
We live LONGER!



Data from United Nations, World Population Prospects, the 2015 Revision

Aging Population

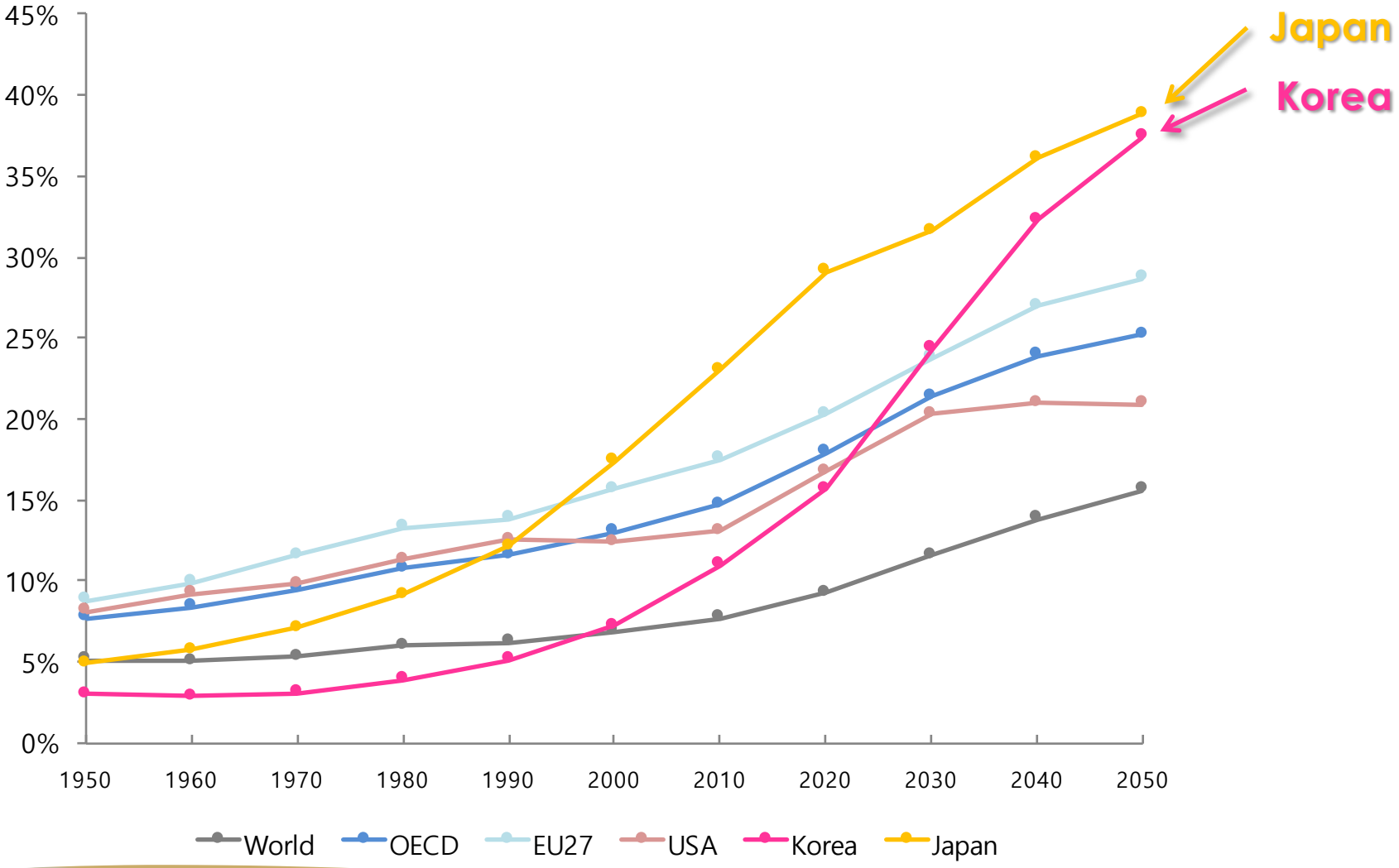
- **Extended life expectancy**
  - Average increase of 20 years during the past few decades (world)
- **Percentage of older population growing**



Source: Petsko, *Genome Biology*, 2008

The vicious cycle will continue,

Increasing proportion of elderly population (65+): 1950-2050



Source: OECD.Stat

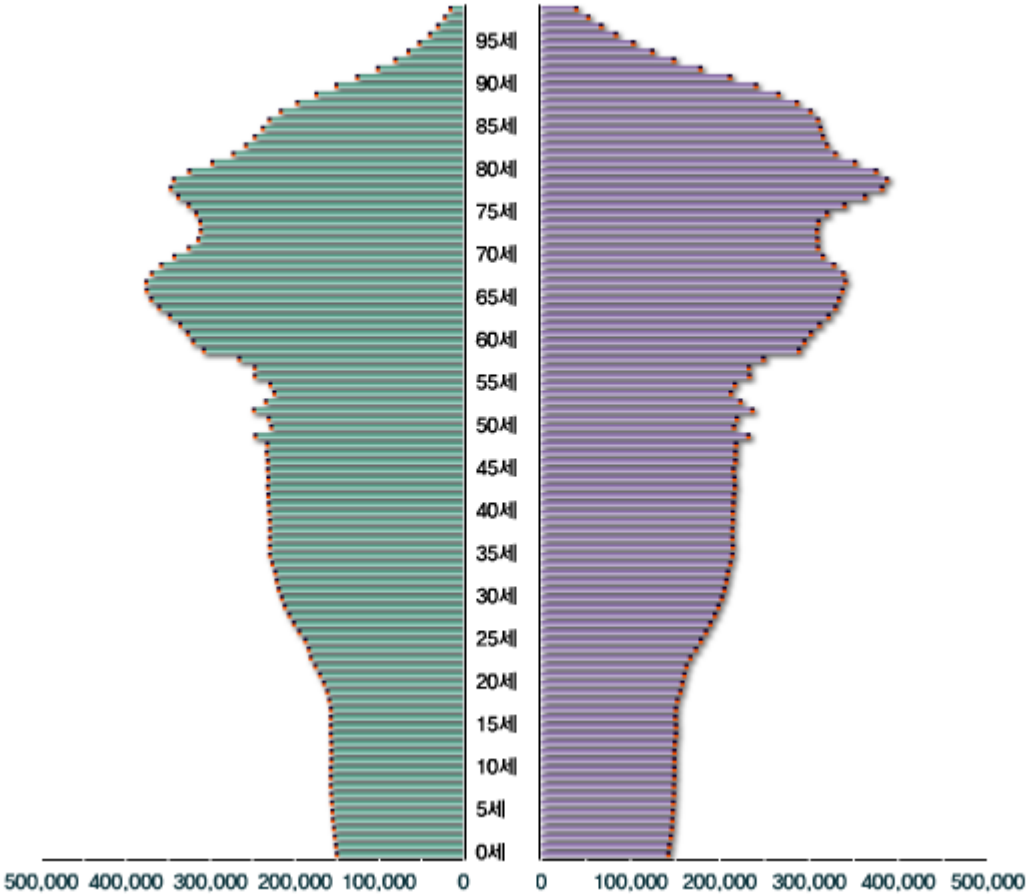
Population Pyramid: Korea 2010-2060

male female

전국

2060

나이(세)	남자(명)
95세이상	148,269
90 - 94	512,651
85 - 89	1,043,430
80 - 84	1,387,526
75 - 79	1,657,375
70 - 74	1,592,416
65 - 69	1,834,825
60 - 64	1,677,470
55 - 59	1,283,235
50 - 54	1,152,691
45 - 49	1,163,270
40 - 44	1,142,632
35 - 39	1,134,928
30 - 34	1,092,197
25 - 29	988,302
20 - 24	862,826
15 - 19	779,873
10 - 14	771,903
5 - 9	770,175
0 - 4	750,602

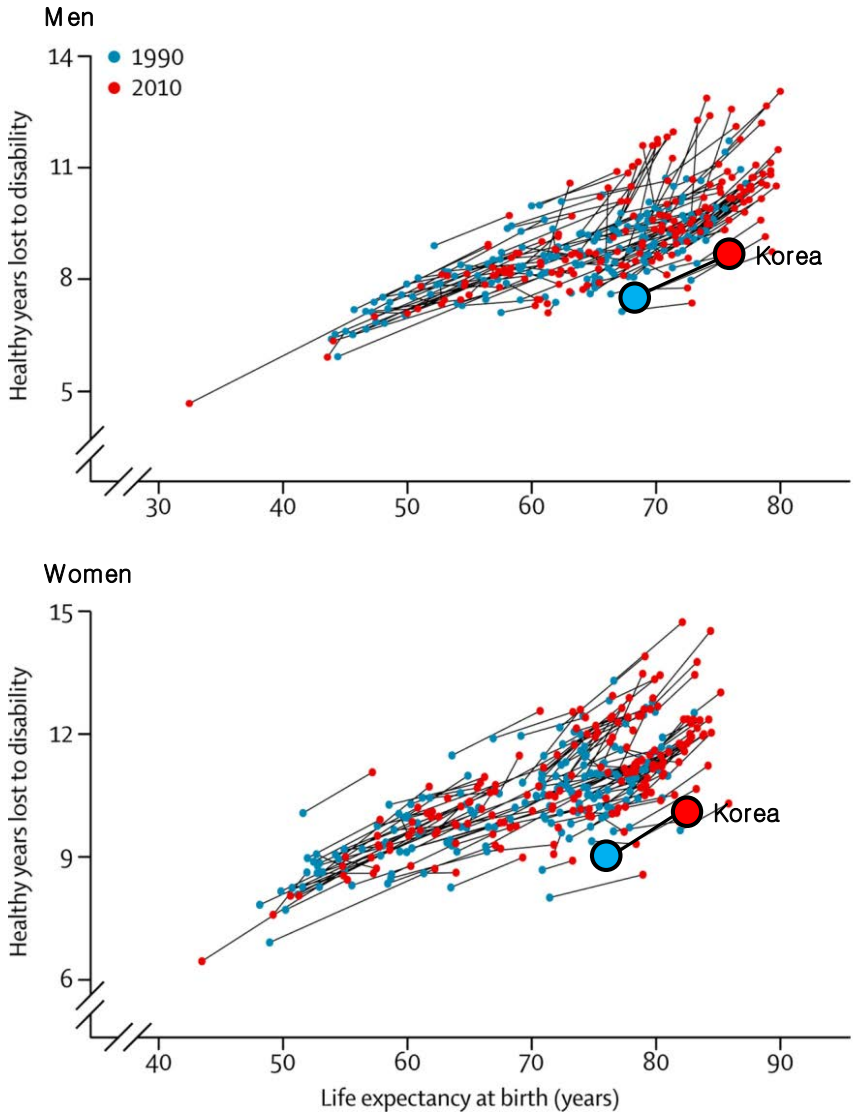


나이(세)	여자(명)
95세이상	334,600
90 - 94	892,213
85 - 89	1,465,023
80 - 84	1,679,894
75 - 79	1,779,851
70 - 74	1,542,363
65 - 69	1,666,825
60 - 64	1,548,357
55 - 59	1,208,913
50 - 54	1,095,532
45 - 49	1,088,810
40 - 44	1,067,956
35 - 39	1,060,312
30 - 34	1,025,175
25 - 29	933,932
20 - 24	809,627
15 - 19	749,137
10 - 14	735,971
5 - 9	730,658
0 - 4	713,347

13% of population age>65 in yr 2015
40% of population age>65 by yr 2060

Population Pyramid, from KOSIS.kr/statPpulation/main.jsp#

BUT…do we live HEALTHIER Life?



Healthy life expectancy (HALE)

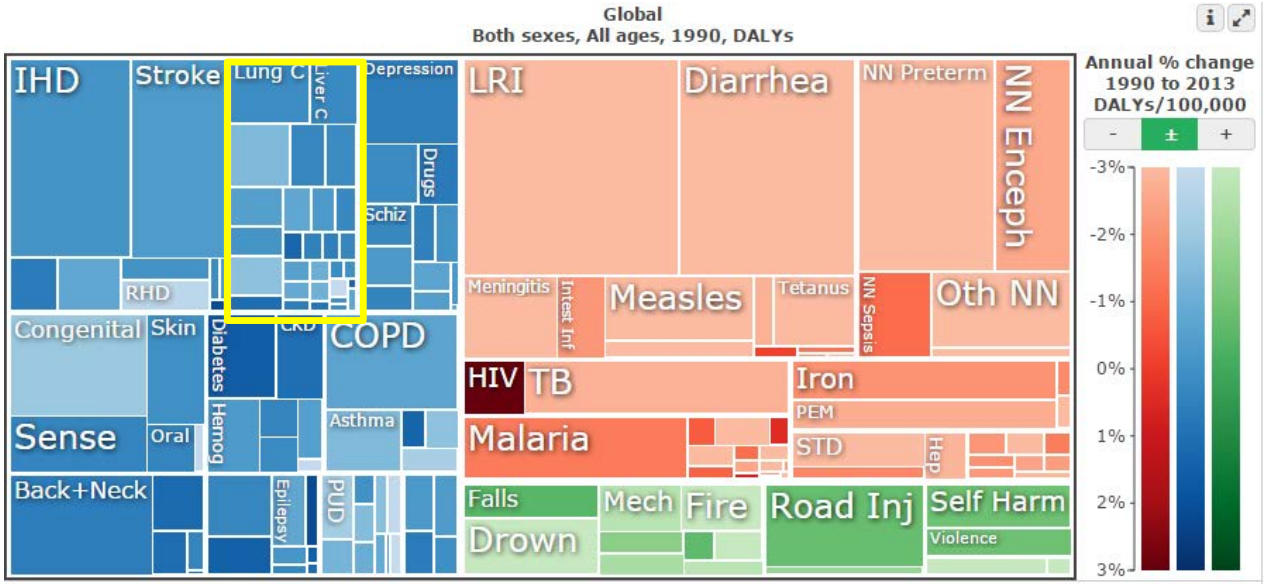
* Average number of years that a person can expect to live in "full" health

Sex	Year	Life Expectancy (LE)	Healthy Life Expectancy (HALE)	Increase in LE	Increase in HALE
Men	1990	68.1	60.6	8.4	7.3
	2010	76.5	67.9		
Women	1990	76.2	67.1	6.5	5.5
	2010	82.7	72.6		

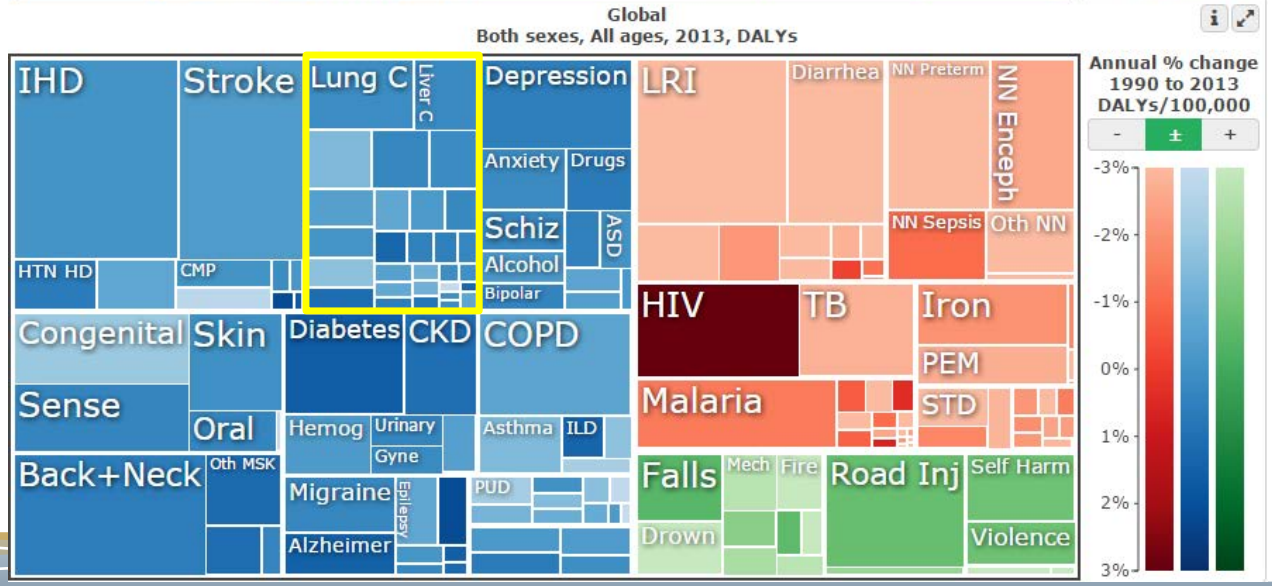
Salomon et al. *Lancet.* 2012

We suffer from chronic diseases!

Global Burden of Diseases (GBD) In 1990



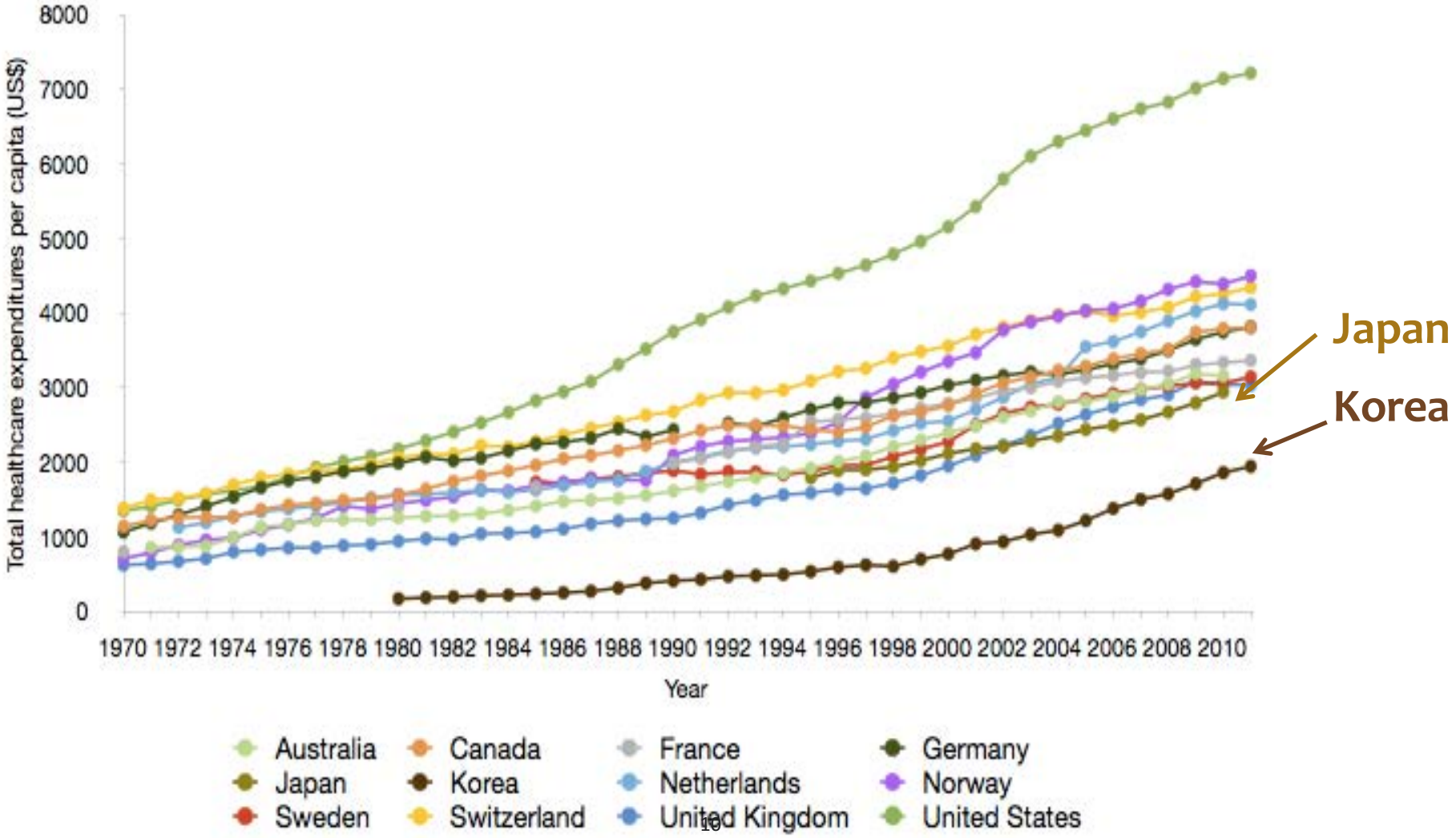
Global Burden of Diseases (GBD) In 2013



Data from GBD 2013 @ http://viz.healthmetricsandevaluation.org/gbd-compare/

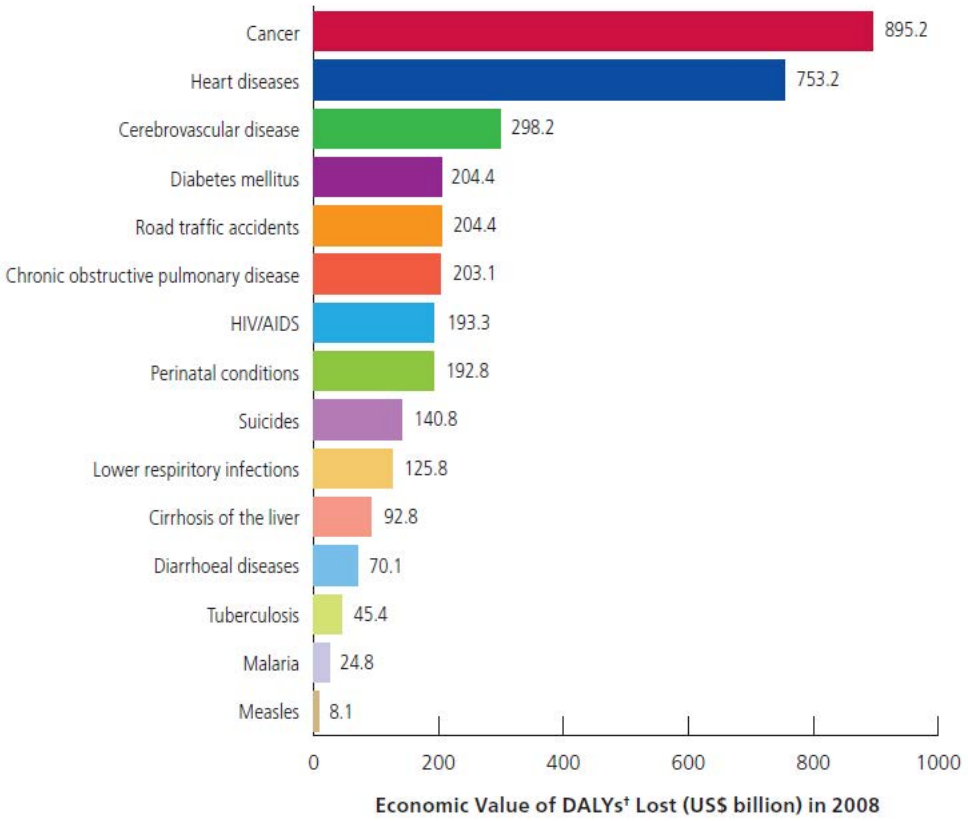
And that comes with it…

- Increased healthcare spending -



Source: OECD Health Data

Economic Loss From the Top 15 Global Causes of Death



†Disability-adjusted Life Year

- Impact of premature death and disability from cancer worldwide was **$895 billion** in 2008
- Represents **1.5% of the world's gross domestic product (GDP)**
- The economic toll from cancer is nearly **19% higher** than heart disease
- The analysis **did not include direct medical costs**

Better, more expensive
Diagnostic tools
Treatment modalities

The Global Economic Cost of Cancer. American Cancer Society. 2011

Unravel the problem

- At its causal origin -

* **Importance of preventive care**
  * *"An ounce of prevention is worth a pound of cure"*
    - Benjamin Franklin

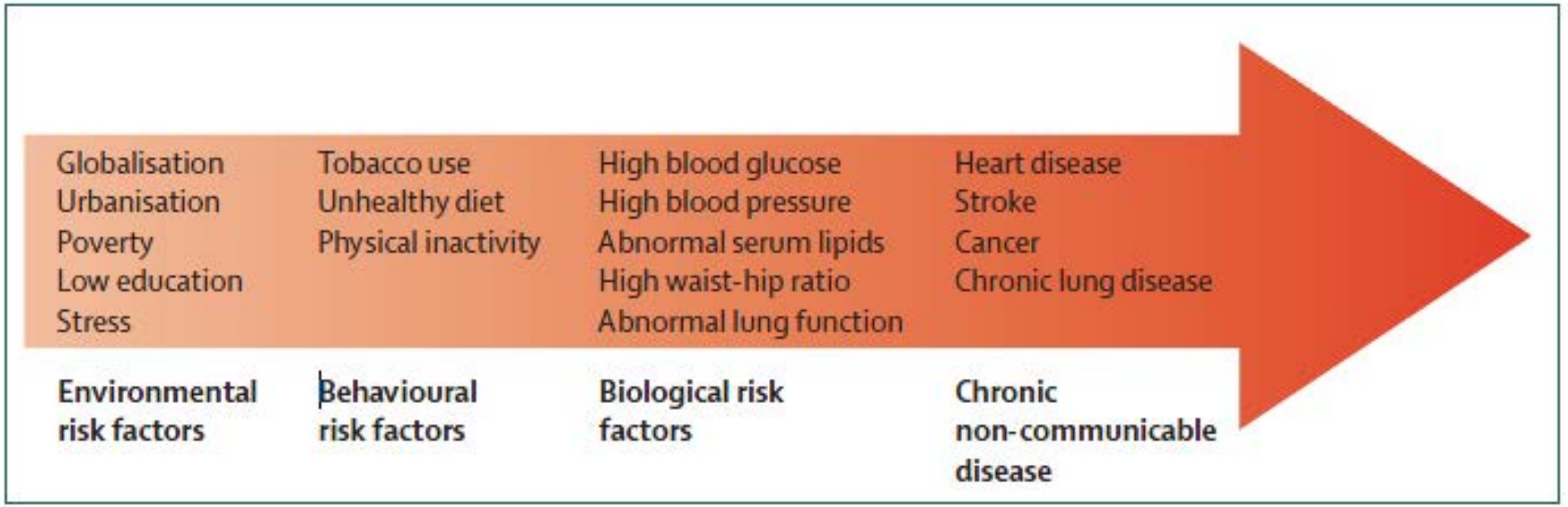
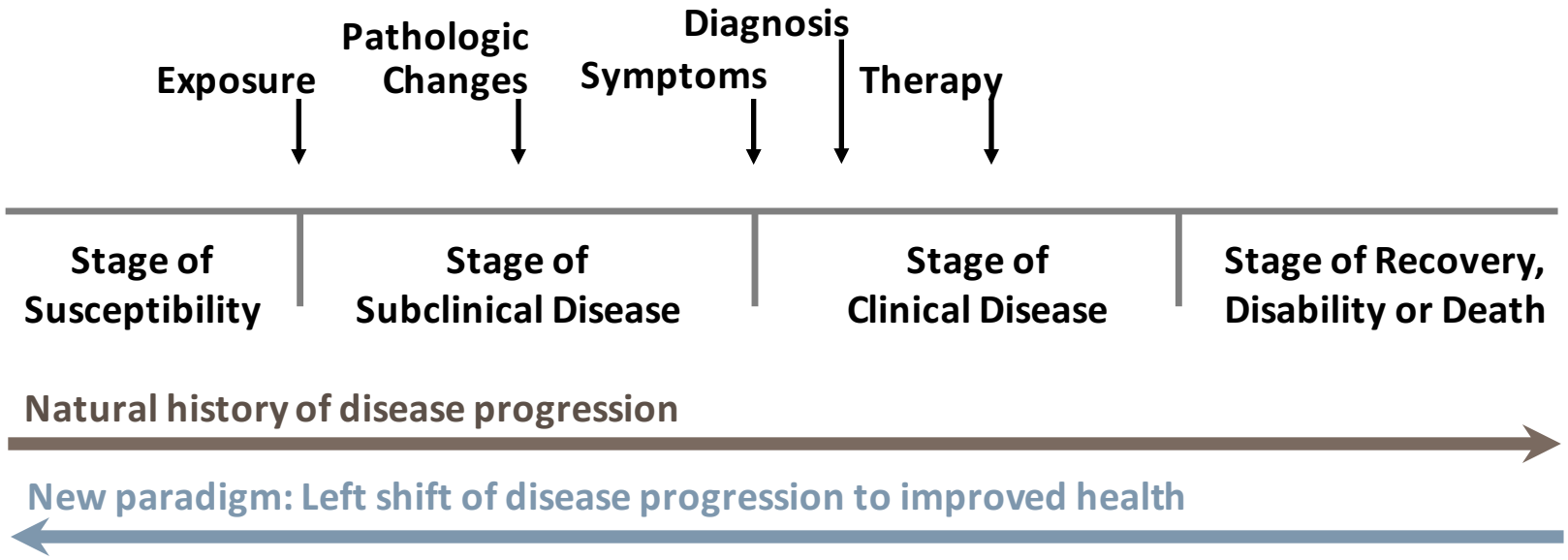


Figure 1: The causation pathway for chronic non-communicable disease

Dans et al. *Lancet.* 2011

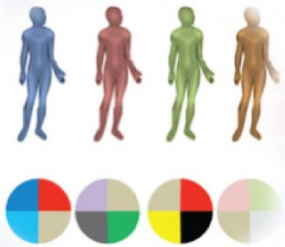
Left shift of natural course of disease



Path to future medicine

Ordinary medicine

Personalized medicine and prevention
via precision and prediction



Governments in Action!

- United States -

Obama calls for major new personalized medicine initiative

REUTERS January 20, 2015 10:03 PM

WASHINGTON (Reuters) - President Barack Obama said in his State of the Union speech on Tuesday that his administration wants to launch a new push to use personalized genetic information to help treat diseases like cancer and diabetes.

Obama urged Congress in his address to boost research funding to support new investments in "precision medicine." "I want the country that eliminated polio and mapped the human genome to lead a new era of medicine – one that

the right treatment at the right time

reverse cystic fibrosis in some patients.

U.S. President Barack Obama delivers his State of the Union address to a joint session of the U.S. Congress ...

Related Stories

1. ...aking first steps on huge precision ...cine project Associated Press
2. Verily, Vanderbilt to test enrollment in U.S. Precision Medicine pilot Reuters

- Launch of a new precision medicine initiative, a $215 million project to collect data on genomes

January, 2015

Dr. Francis Collins, *NIH Director:*

"…empower any person, anywhere in the U.S." in what's called the **PMI Cohort Program**

"NIH will provide funding to Vanderbilt U. [for a collaborative pilot project] with Verily (former Google Life Sciences)"

- Obama to ask Congress for $309 million [in 2017 for the initiative scale up]
- A massive database will track at least 1 million volunteers by 2019

February, 2016

NIH taking first steps on huge precision medicine project

AP By LAURAN NEERGAARD
February 25, 2016 1:40 PM

WASHINGTON (AP) — President Barack Obama held out the promise of medical break-

http://news.yahoo.com/obama-calls-major-personalized-medicine-initiative-030325518.html
http://news.yahoo.com/nih-taking-first-steps-huge-precision-medicine-project-111203692--politics.html

Dr. Francis Collins at SNUH

Building a Large U.S. Cohort for Precision Medicine Research

- NIH Workshop, February 11-12, 2015
- Representatives from a wide variety of fields
- Major areas of focus:
  - Cohort identification and participant recruitment
  - Participant engagement, data privacy, and novel ways of returning information to participants
  - Data collection, including mobile technologies
  - Informatics and electronic health records

Precision medicine in Korea
- Ministry of Health and Welfare -

Core area	Project	Department
Infrastructure establishment for precision medicine cohort	New precision medicine cohort	Cohort
	Enhance existing cohort and biobanks	
Prepare systemic coordination for precision medicine-based big data	Standardization and linkage of genomic-medical data	Medical record and public health based big data
	Establishment of open data hub	Information security and standardization
Develop precision medicine based health services	Development of precision medicine based artificial intelligence	Public health big data
	Precision medicine based clinical experiment system	Omics
	Development of precision medicine based healthcare service model	Mobile health care
Improve policies and laws related to precision medicine and develop manpower	Improvement of laws, policies, and regulations	Law/Policy
	Train professionals in the field of precision medicine	

The use of "Korean Chip" will help realize precision medicine in Korea:

* Genomic information on 100,000 Koreans
* Linkage with core infrastructure such as cohort, healthcare industry, electronic health records, and big data

* **National Cancer Center (NCC): Large-scale cancer precision medicine cohort**
  * Genetic data of 1 million cancer patients
  * Provide basis for development of chemotherapeutic agents
  * Big data driven prevention of cancer recurrence

국립암센터 NATIONAL CANCER CENTER

Source: Korea Health Industry Development Institute

Precision medicine in Academia
- Seoul National University Bundang Hospital -

Healthcare Innovation Park (HIP) &
Seoul National University Bundang Hospital (SNUBH)

- Seoul National University Bundang Hospital (SNUBH) to lead Big Data-based precision medicine in Korea, a new leap since its embark as the nation's first fully digitalized, paperless hospital

- Established task force for collaborative research on precision medicine

Chul-Hee Lee, *SNUBH President & CEO*:

"The realization of precision medicine for each and every patient may be advanced through the integrated use of hospital database system and genomic information."

October, 2015

Part II.

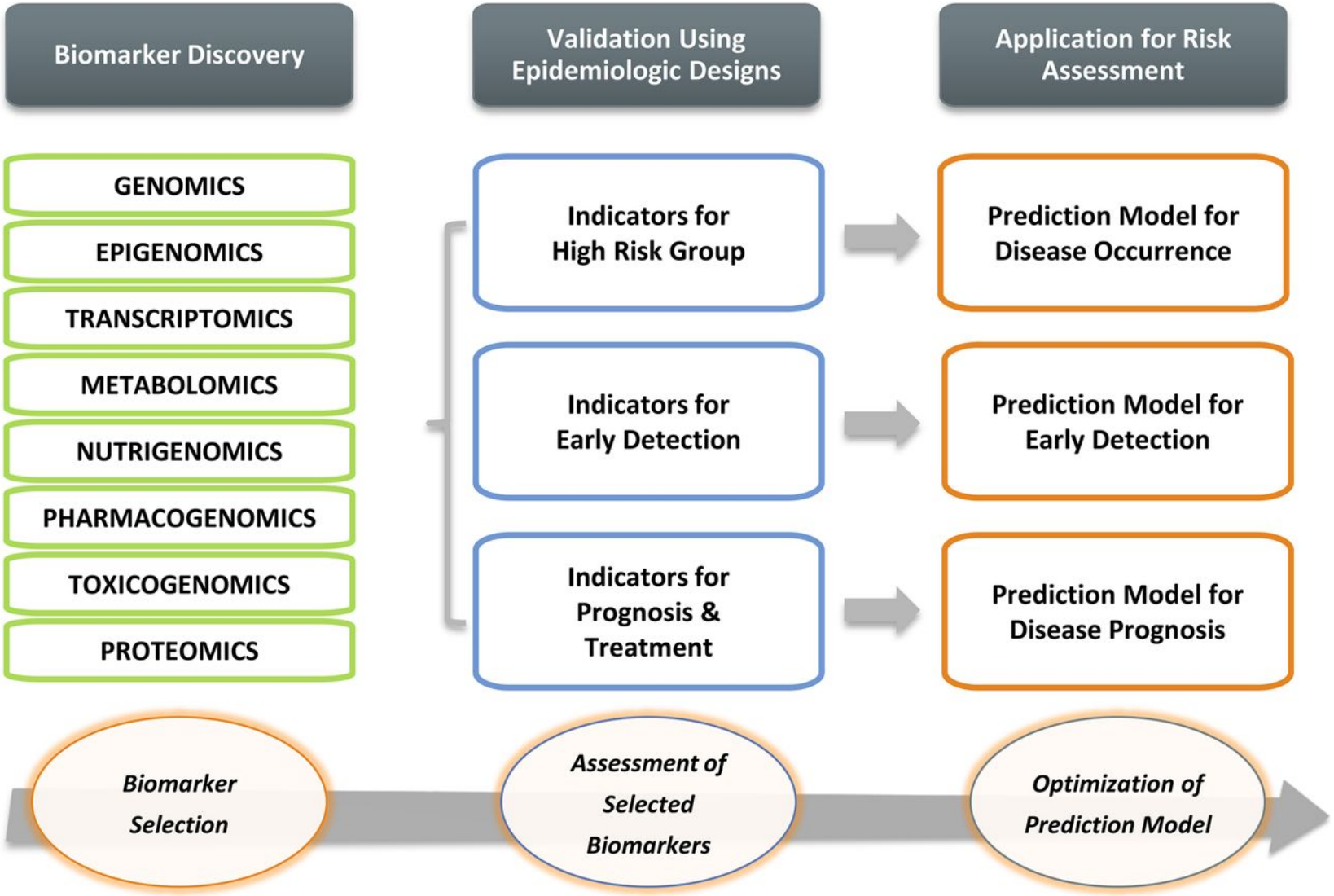
Evidence of personalized preventive research on cancer

Today, it's all about prediction

New paradigm shift: AJCC's prognostic, statistically based risk calculators in 2016

- *Cancers to be evaluated:*
  - *breast, colon, prostate, lung, melanoma, head & neck*
- *For each cancer type, risk models must:*
  - *Predict overall survival or death*
  - *Pass all 16 criteria (13 inclusion + 3 exclusion)*

Risk prediction using biomarkers

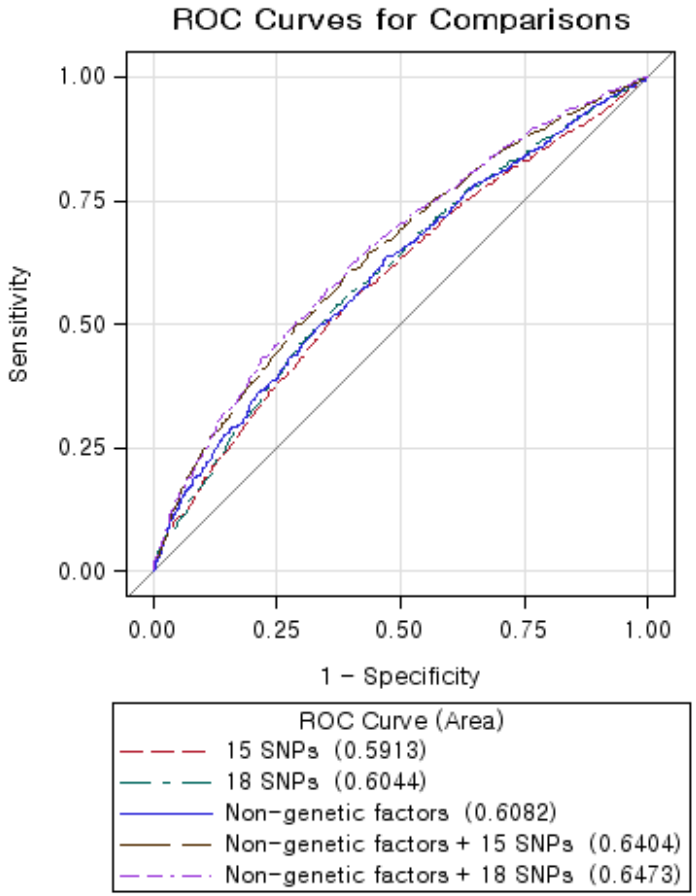


Song, Lee and Kang , *JJCO*, 2014

Seoul Breast Cancer Study (SeBCS)

Discriminative values of breast cancer risk models using genetic and non-genetic factors from Seoul Breast Cancer Study (SeBCS)

- Number of Subjects (2001-2007)
  - Cases: 4040
  - Controls: 3946
- Original papers (2003~2012)
  - SeBCS: 51 papers
  - Collaboration: 24 papers




SNUH


AMC


Borame hospital


EUMC


Community-based

An example of breast cancer survival prediction

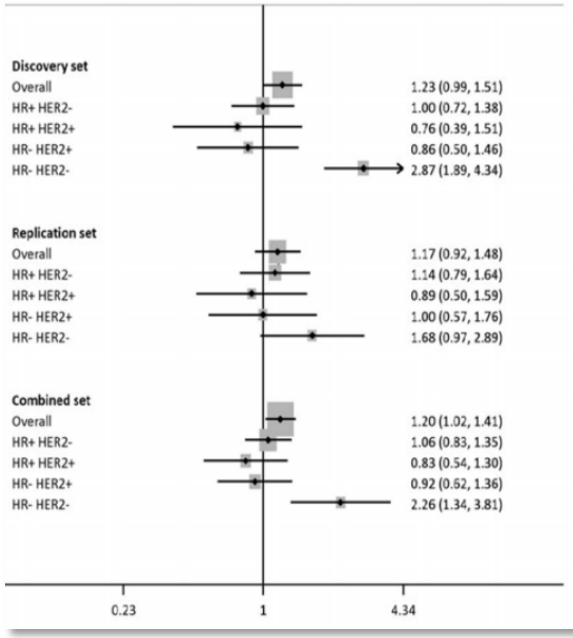
PLOS ONE

RESEARCH ARTICLE

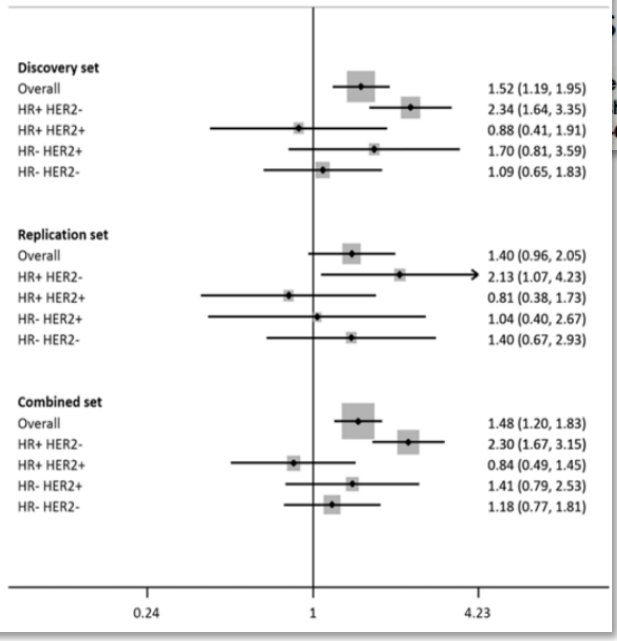
Prediction of Breast Cancer Survival Using
nd Genetic Markers by Tumor

ob Choi[1,2,3☯], Hyuna Sung[2,4], Sujee Jeon[3], Seokang Chung[2], Sue
hik Han[1,5], Jong Won Lee[6], Mi Kyung Kim[7], Ji-Young Lee[8], Keun-
Ghee Han[9], Sei-Hyun Ahn[6], Dong-Young Noh[1,5], Daehee Kang[1,2,3]*

A. Tumor subtype: rs166870



B. Tumor subtype: rs10825036



- Overall:
  - Harrell's $C_{clinical\ model}$ = 70.92%
  - Harrell's $C_{combined\ model}$ = 71.37%
  - p = 0.03
- HR+ HER2-:
  - Harrell's $C_{clinical\ model}$ = 65.08%
  - Harrell's $C_{combined\ model}$ = 66.69%
  - p<0.01
- HR- HER2-:
  - Harrell's $C_{clinical\ model}$ = 63.26%
  - Harrell's $C_{combined\ model}$ = 65.88%
  - p<0.01

Comparison of the **predictive powers** of disease-free survival (DFS) for breast cancer:

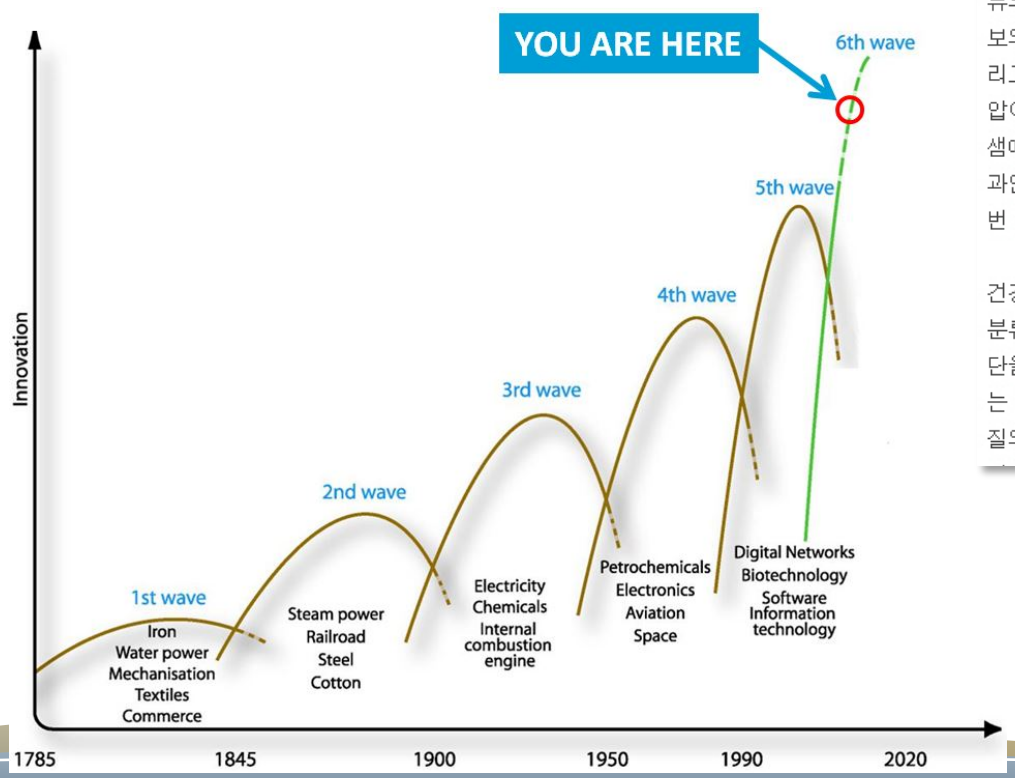
- *Model with **combined clinical (age, TNM stage, tumor subtype) and genetic variables** tended to have better predictive powers overall*
- ***Genetic factors played role in distinguishing high and low risk groups** when using combined prognostic markers*

Song, Kang et al., *PLoS One*, 2015.

Part III.

Preparation for future needs

The speed of knowledge accumulation



[열린세상] 건강정보 홍수시대/강대희 서울대 의대 예방의학 학장

좋아요 1 +1 0 목록 메일 인쇄 글씨크기

우리는 건강 관련 정보의 홍수시대에 살고 있다. 주요 일간지, 방송매체, 의학 관련 전문지에서는 다양한 종류의 건강 관련 정보를 쉴 새 없이 쏟아내고 있다. 정보의 진위를 떠나 우리는 너무 많은 건강정보에 시달리고 있다. 최근 '하루에 커피를 4잔 이상 마시면 고혈압이 예방된다'는 연구 결과가 나왔다. '토마토가 전립샘에 좋다' '채소와 과일 섭취는 폐암을 예방한다'는데 과연 믿을 만한 것인지, 어떤 연구에서 나온 것인지 한번 살펴보자.

▲ 강대희 서울대 의대 예방의학 학장

건강정보를 만들어 내는 의학연구는 크게 세 종류로 분류된다. 동물이나 세포를 이용한 실험연구, 인구집단을 장기간 관찰해 질병 발생에 관여하는 원인을 찾는 코호트 연구 등의 역학 관찰 연구, 신약이나 예방물질의 효과를 검증하는 임상·예방시험 연구로 나뉜다.

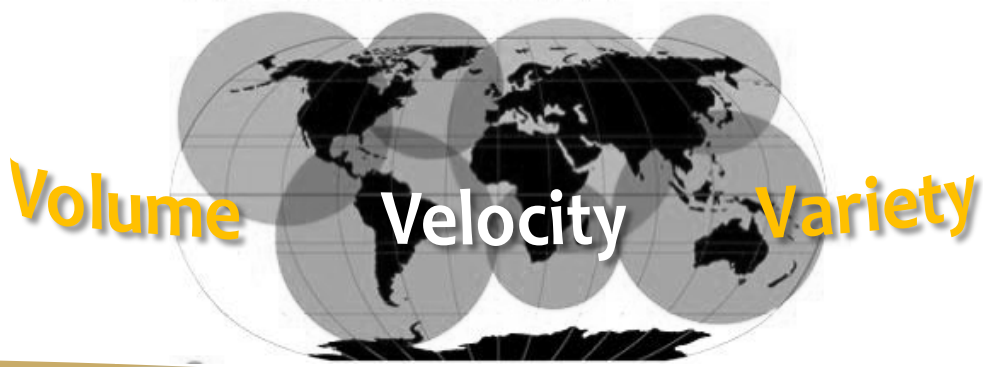
Smaller world, bigger data

Wired world (the Internet)

Global transportation network

Infinite accumulation of data with database technology

More knowledge and insight



Source: IBM 2013 @ https://www-304.ibm.com/connections/blogs/ibmx86/entry/biginsights_for_big_data?lang=ko

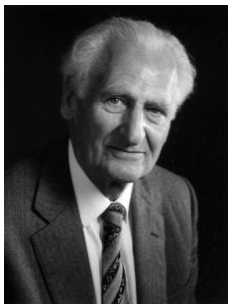
Collaborative work is important in the future

- **The art of communication and teamwork**
  - With professionals from various sectors
  - Within a global setting

A next generation large genomic cohort in Korea

In Need of a *Next Generation* Cohort

Examples of Previous Cohorts



The Nurses' Health Study

NATIONAL CANCER INSTITUTE
PLCO
Prostate, Lung, Colorectal, & Ovarian
CANCER SCREENING TRIAL

Next Generation Cohort

- Need more ***power***
- Outcome ***heterogeneity***
- ***Gene-environment interaction***
- ***Wider distribution*** of exposure variables

Taking Advantage of Korea's *Unique Environment*

- ***Biennial*** Health Examination ***by Law*** (National Health Insurance Corporation)
- National ***Personal Identification*** System (13-digit residence registration number)

➔ **Automatic Repeated Follow-up & Possible Integration to Secondary Data**

Birthday (6)
YYMMDD

—

Registration (7)
Sex-Birth place-Order-Hidden

Identification Card

Driver's license

Passport

HEXA (Health Examinees Study) since 2004

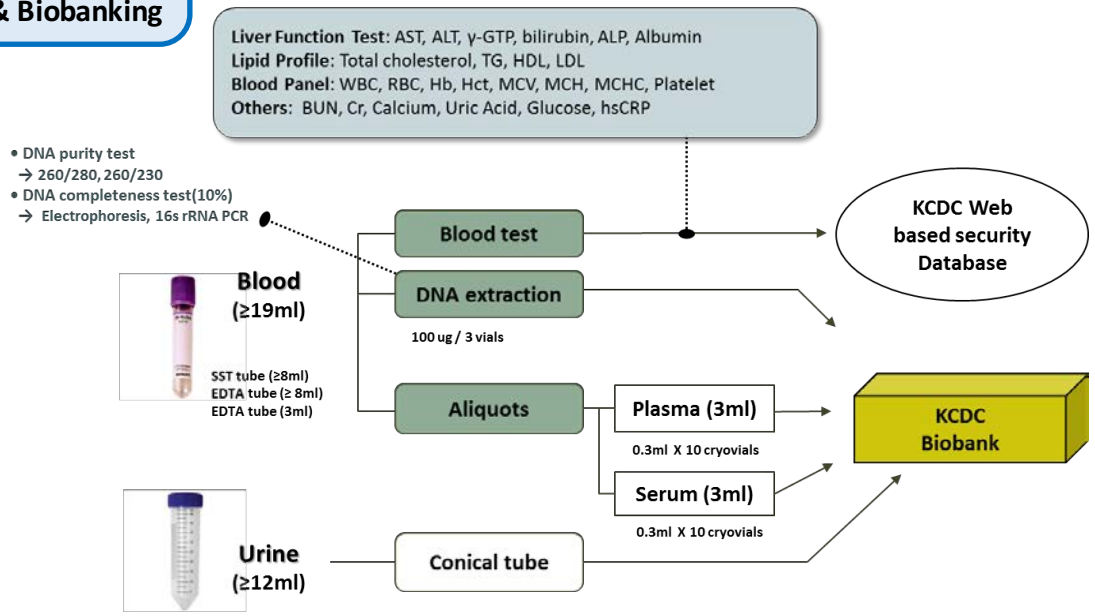
38 Participating Health Examination Centers

- Representing the community
- Built-in infrastructure for repeated survey
- Considered to have f/u rate of 50% or more
- Experience of multicenter network research

✓ *Adult men and women*
✓ *40-69 years of age*
✓ *Health examination center visitors*

Subject Recruitment

Centralized Database Storage & Biobanking



HEXA subjects recruit 2004-2012 (n=162,142)

- **Men: Women = 2:1**
- **Mean age at recruitment (years)**
  - Men: women = 53.7 (±8.2): 52.6(±7.6)

Composition of HEXA Questionnaire & Lab data

- **Total number of questionnaires n=1,303**
  - SES, Past medical history, lifestyle habits, socio-psychological factors, reproductive factors, dietary habits (including 106 SQ-FFQ)
  - Clinical & physical examination

Estimated Number of Incident Cases of Selected Diseases

Disease Group	2018	2023
All-site cancer	11,749	17,800
Ischemic heart disease	2,663	4,034
CVA	6,308	9,556

HEXA research activities

DOI:http://dx.doi.org/10.7314/APJCP.2015.16.4.1591

Rationale and Design of the Health Examinees Study in Korea

J Epidemiol 2015
doi:10.2188/jea.JE20140136

PLOS ONE

Contents lists available at ScienceDirect

Journal of Affective Disorders

Jung et al. BMC Pregnancy and Childbirth (2015) 15:228
DOI 10.1186/s12884-015-0665-2

BMC Pregnancy & Childbirth

RESEARCH ARTICLE Open Access

Original Article

Journal of Preventive Medicine

PLOS ONE

RESEARCH ARTICLE

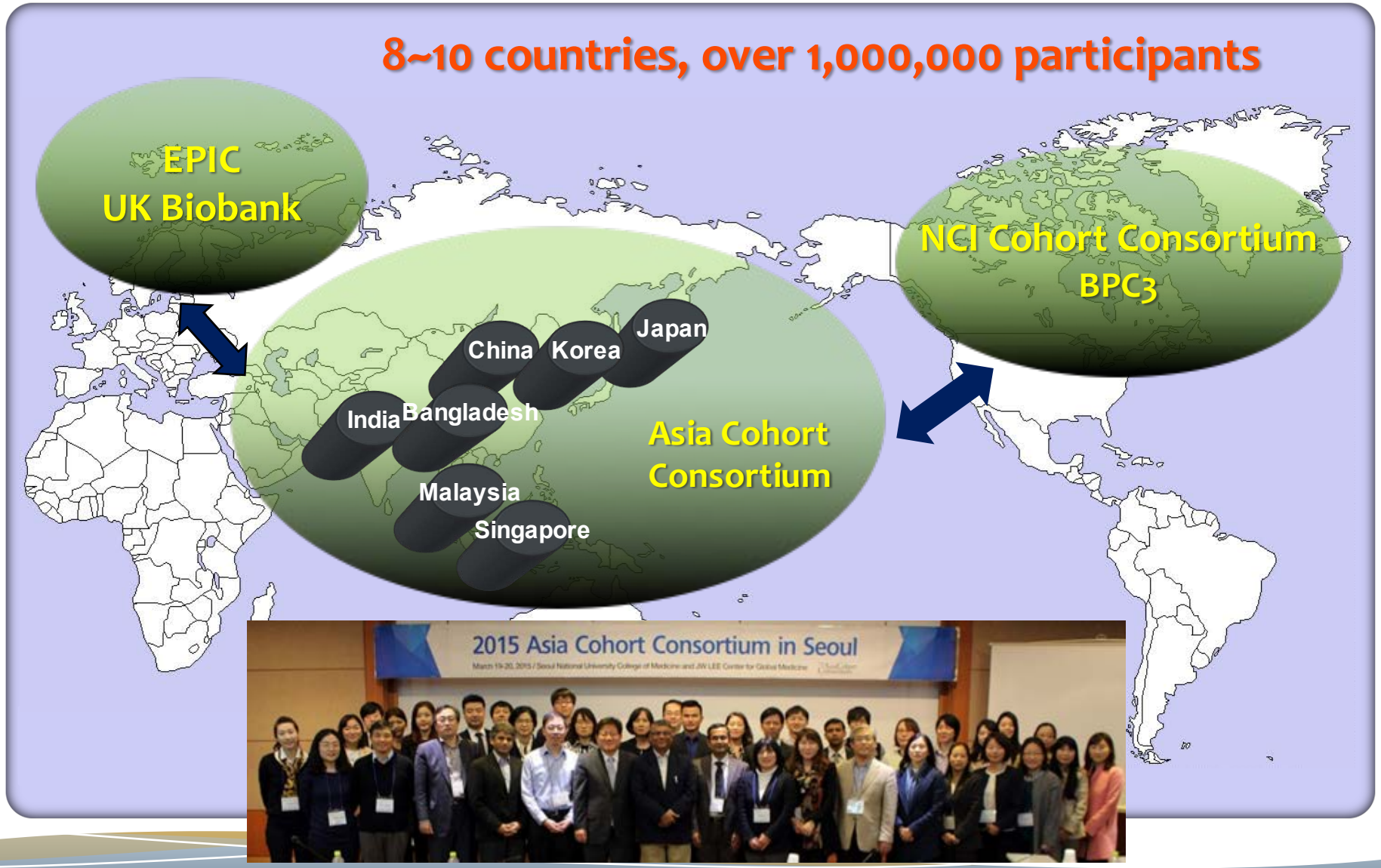
What Are the Major Determinants in the Success of Smoking Cessation: Results from the Health Examinees Study

Jae Jeong Yang[1,2], Minkyo Song[1,2,3], Hyung-Suk Yoon[1,2,3], Hwi-Won Lee[1,3], Yunhee Lee[1,3], Sang-Ah Lee[4], Ji-Yeob Choi[1,3,5], Jong-koo Lee[6,7], Daehee Kang[1,2,3,5]*

Why Asia?

- 2/3 of world's population
- 4/5 of new cancer occurrence by 2020
- Wider distribution of exposure variables in relatively homogenous ethnic backgrounds
  - smoking, diet, environment
- Rapid changes in certain personal habits
  - reproductive factors, urbanization, etc.

Asia Cohort Consortium (ACC)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ART

As

OPEN ACCESS Freely available online

Body Mass Index an
Pooled Analysis of 9
Consortium

Paolo Boffetta[1,2], Dale McLerran[3], Chandra Gupta[4], Renwei Wang[13], Chen[17,18], Jian-M Mangesh Surya Xiang[11], Masato Park[27], Chen-Ya Zheng[12], John D

origina

Body m
of canc
over 50

P. Boffetta[1,2], X. O. Shu[9], E S. Tsugane[6], C. J. Chen[17], B. Rolland[3],

[1]The Tisch Cancer Ins Lyon, France; [2]Divisio School of Medicine, M Research Center for C China; [3]Department o Department of Medici Epidemiology, Radiati Graduate School of M Academia Sinica and College of Medicine, Seoul, Korea; [17]Genom Taiwan; [18]Department Biomedical Science, S Center, The University Cancer Institute/Hospa Zealand

Received 12 August 20

Abstract

Background: Th has the prevale causes of diabet been adequatel

Methods and body mass inde over 900,000 inc regression mod adjustment for sex- and age-a participating co confidence inte The positive ass population, alth cohorts from In 0.03); no differe

Conclusions: Th Asian populatio

Associatio
pancreas c
Consortiu

Yingsong Lin[2], Prakash C. G Shoichiro Tsu Kotaro Ozasa[1] Keun-Young Y Catherine Sau Waka Ohishi[C] San-Lin You[I,II] Betsy Rolland Mark Thornqu

We aimed to examine risk of death from par data from the Asia Co pooled analysis includ cohort studies in Asia models were used to confidence intervals fo to BMI. Seven predefi 20.0–22.4, 22.5–24.9, 2 the analysis, with BMI group. The multivariab risk factors, including a We found no statistica between each BMI ca pancreas cancer in all the risk of mortality in Age, smoking, and a h association between E cancer. In planned sub an increased risk of de with a BMI less than 18 a history of diabetes; ha interval: 1.01–4.00) (*P* fo support an association from pancreas cancer in these A

Journal of Cancer Prevention 22:2
Kluwer Health | Lippincott Willian

Meat intake and
prospective coh

OPEN ACCESS Freely available online

PLOS | MEDICINE

Burden of Total and Cause-Specific Mortality Related to ...ars in Asia:

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Original Contribution

Associations of Body Mass Index, Smoking, and Alcohol Consumption With Prostate Cancer Mortality in the Asia Cohort Consortium

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Many potentially modifiable risk factors for prostate cancer are also associated with prostate cancer screening, which may induce a bias in epidemiologic studies. We investigated the associations of body mass index (weight (kg)/height $(m)^2$), smoking, and alcohol consumption with risk of fatal prostate cancer in Asian countries where prostate cancer screening is not widely utilized. Analysis included 18 prospective cohort studies conducted during 1963–2006 across 6 countries in southern and eastern Asia that are part of the Asia Cohort Consortium. Body mass index, smoking, and alcohol intake were determined by questionnaire at baseline, and cause of death was ascertained through death certificates. Analysis included 522,736 men aged 54 years, on average, at baseline. During 4.8 million person-years of follow-up, there were 634 prostate cancer deaths (367 prostate cancer deaths across the 11 cohorts with alcohol data). In Cox proportional hazards analyses of all cohorts in the Asia Cohort Consortium, prostate cancer mortality was not significantly associated with obesity (body mass index >25: hazard ratio (HR) = 1.08, 95% confidence interval (CI): 0.85, 1.36), ever smoking (HR = 1.00, 95% CI: 0.84, 1.21), or heavy alcohol intake (HR = 1.00, 95% CI: 0.74, 1.35). Differences in prostate cancer screening and detection probably contribute to differences in the association of obesity, smoking, or alcohol intake with prostate cancer risk and mortality between Asian and Western populations and thus require further investigation.

alcohol drinking; Asia; mortality; obesity; prostate cancer; prostate-specific antigen; smoking

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Asia Cohort Consortium

- Challenges for collaborative research -

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Review Article

Asia Cohort Consortium: Challenges for Collaborative Research

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ABSTRACT

In this era of chronic diseases, large studies are essential in investigating genes, environment, and
interactions as disease causes, particularly when associations are important but not strong. M
expansion and generalization of the results, studies should be conducted in populations outside
Here, we briefly describe the Asia Cohort Consortium (ACC), a collaborative cancer cohort re
was first proposed in 2004 and now involves more than 1 million healthy individuals acros
approximately 50 active members from Bangladesh, China, India, Japan, Korea, Malaysia, S
Thailand, the United States, and elsewhere. To date, the work of the ACC includes 3 articles publis
roles of body mass index, tobacco smoking, and alcohol consumption in mortality, diabetes, and c
intestine. Many challenges remain, including data harmonization, resolution of ethical and legal iss
of protocols for biologic samples and transfer agreements, and funding procurement.

Key words: Asia; cohort; consortium

Challenges:

- *data harmonization*
- *resolution of ethical and legal issues*
- *establishment of protocols for biologic samples and transfer agreements*
- *funding procurement*
- *precise exposure assessment*

INTRODUCTION

Prospective cohort studies provide the best level of observational evidence on disease causation. Furthermore, prospective cohort studies have specific strengths over clinical trials, which are often regarded as more powerful than observational studies in the hierarchy of evidence. For instance, in situations where it is unethical to design an experimental study (eg, in situations involving exposure to tobacco, alcohol, or obesity), observational studies are the only way to undertake research. Further, unlike clinical trials, cohort studies can assess multiple outcomes for any 1 exposure or multiple exposures for a specific outcome. Chronic diseases are on the rise worldwide, and Asian countries face a growing disease burden and the many

Since the completion of the Human Genome Project, epidemiologic studies encompassing genetics have prospered, and the importance of prospective cohorts has been more widely recognized.[5] Moreover, a sufficiently large cohort or a population laboratory is essential for understanding the roles of genetic variation, environmental exposures, and the interaction between genes and exposures in the development of a disease.[6] Analyses of gene–environment interactions in complex diseases with small interaction odds ratios or of genome–environment-wide interactions require even larger sample sizes to confirm associations.[7,8] Potter has suggested that a cohort of at least 1000000 ethnically diverse individuals ("the Last Cohort") is essential to discover disease susceptibility, early-detection biomarkers, and more-precise phenotypes.[9]

Song, Kang et al, *J Epidemiol* 2012

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