Ministry of Education, Culture, Sports and Technology
Human Resources Development Program

Division of Clinical and Bioinformatic Engineering
Department of Clinical Bioinformatics

Graduate School of Medicine, The University of Tokyo
Open Lecture Courses 2003

Undergraduate/ Graduate (Medicine, Engineering, Biology), Continuing Education

Other Bioinformatics Human Resources Development Units

Research Organization, Company, Medical Institution

Qualified Personnel

Partnership

Human Resources Supply

Doctor of Medicine, Doctor of Health Sciences, Master of Medicine, Master of Health Sciences, Doctor of Engineering, Master of Engineering, Clinical Research Coordinator, Health Information Manager, Medical Information Engineer

Division of Clinical and Bioinformatic Engineering

Statistical Genetics

Clinical Medicine (providing environment for research)

Biostatistics

Clinical Epidemiology

Clinical Information Engineering

Providing IT Related Courses
Dispatching Qualified Personnel

Division of Clinical Genome Science

Division of Clinical Epidemiology

Division of Clinical and Bioinformatic Engineering

Private Corporations

Dpt. of Human Genetics

Dpt. of Cardiovascular Internal Medicine

Dpt. of Diabetes & Metabolism Internal Medicine

Dpt. of Biostatistics, Epidemiology

Dpt. of Pharmaco-epidemiology

Dpt. of Planning, Information & Management

The University of Tokyo Hospital,
Graduate School of Medicine and Faculty of Medicine, the University of Tokyo

- **CBI Web site**

  http://cbi.umin.ne.jp
- **Applications and inquiries**

  Email：cbi-secretary@umin.ac.jp

  TEL：03-5800-9845

  FAX：03-5800-9848

Open Lecture Courses (2003)

- **Introduction to Clinical Medicine** : **Twenty meetings;**
  (Meets with "Human and Engineered Environmental Studies") **Apr-Jun, Oct-Nov**
- **Introduction to Clinical Epidemiology** : **Twelve meetings; Jun-Sept**
- **Medical Science and Nursing Science** : **Eight meetings; Oct-Nov**
- **Biomedicine** : **Eight meetings; Mar**
- **Genome Information** : **Ten meetings; Jun-Jul**
- **Introduction to Clinical Information Engineering** : **Ten meetings; Sept, Nov-De**
- **Clinical Information Management** : **Ten meetings; Dec-Jan**
- **Clinical Information Systems Engineering** : **Ten meetings; Jan-Feb**

- **Intensive Courses (Eight Subjects)**

- **Introduction to Healthcare Administration** : **Eight meetings;**
  (Pharmaco Business Innovation Contribution Lecture) **to be announced**

- **Pre-registration (starts one month before the first class) is required.**
- **Issue diploma for each course. (Required attendance: 80% or more)**
- **Full-year courses are offered free of charge on SKY PerfecTV Medical & Welfare channel 774.**
- **Acquire recognition as accredited units at graduate schools/universities.**

Intensive Courses

- **Introduction to Statistics Package (SAS1)：four meetings (completed)**
- **Introduction to Statistics Package (SAS2)**
- **Introduction to Statistics Package (JMP)**
- **Introduction to Methodology of Epidemiology**

  (Meets with “Special Lecture on Epidemiology & Preventive Health Science I”)：six meetings
- **Introduction to Multivariate Analysis：three meetings**
- **Clinical Tests Methodology**
- **Medical Writing**
- **Introduction to Social Medicine**

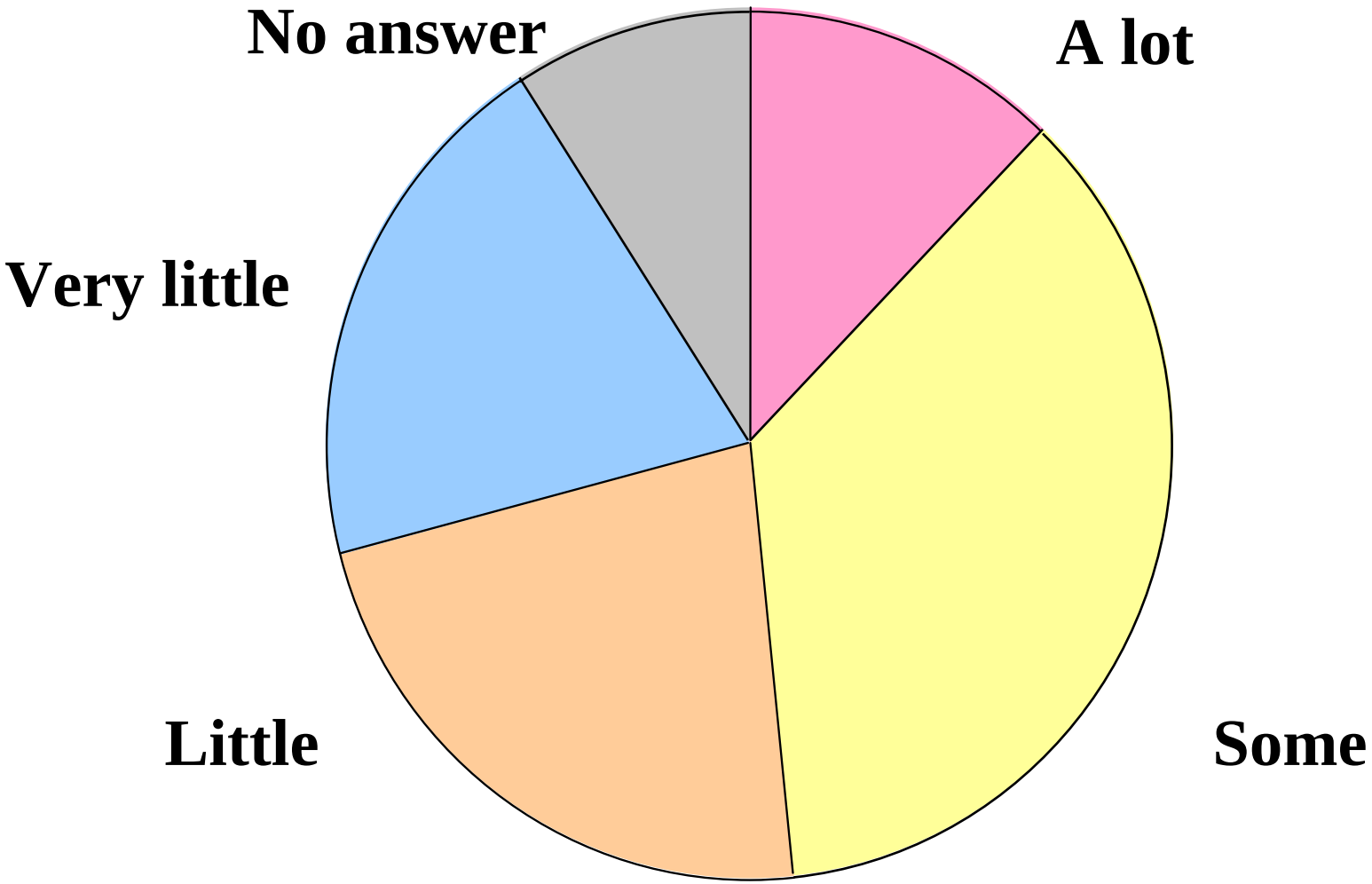
-Clinical Information Systems Data Analysis- : six meetings

Calendar for Introduction to Clinical Medicine (Instructor)

(All meetings held at 6pm on Tuesdays at Clinical Lecture Hall)

(1)	April 22	-1-	General Medicine – from Clinical Viewpoint (Tsutomu Yamazaki)
(2)	April 22	-2-	General Medicine – from Cell to Human Anatomy (Ichiro Manabe)
(3)	May 6	-1-	Kidney, Metabolism, Endocrine 1 – Diabetes (Kazuo Hara)
(4)	May 6	-2-	Radiation, Diagnostic Imaging (Tadashi Yamazaki)
(5)	May 13	-1-	Cardiovascular Disease 1 – Hypertension (Dobun Hayashi)
(6)	May 13	-2-	Neurological Disorder – Ischemic & Hemorrhagic Strokes (Yoshio Momose)
(7)	May 20	-1-	Cardiovascular Disease 2 – Arrhythmia, Neurophysiological Tests (Toru Suzuki)
(8)	May 20	-2-	Kidney, Metabolism, Endocrine 2 – Obesity, Hyperlipidemia (Kazuo Hara)
(9)	May 27	-1-	Cardiovascular Disease 3 – Cardiac Hypertrophy, Heart Failure (Koshiro Monzen)
(10)	May 27	-2-	Cardiovascular Disease 4 – Arteriosclerosis, Myocardial Infarction (Ichiro Manabe)
(11)	June 3	-1-	Kidney, Metabolism, Endocrine 3 – Endocrinopathy (Yasushi Imai)
(12)	June 3	-2-	Kidney, Metabolism, Endocrine 4 – Renal Disease, Dialysis (Toru Hosoda)
(13)	Oct. 28	-1-	Gastrointestinal Disorder 1 – Gastrointestinal Tract, Stomach, Colon (Tadashi Yamazaki)
(14)	Oct. 28	-2-	Gastrointestinal Disorder 2 – Liver, Gallbladder, Pancreas (Koshiro Monzen)
(15)	Nov. 4	-1-	Laboratory Test – Blood Test, Biochemistry (Toru Suzuki)
(16)	Nov. 4	-2-	Infection (Bacteria, Virus) (Toru Hosoda)
(17)	Nov. 11	-1-	Blood – Mechanism of Hematopoiesis and Anemia, Leukemia (Yasushi Imai)
(18)	Nov. 11	-2-	Allergy, Connective Tissue Disorder – Immunity and Disease (Tadashi Yamazaki)
(19)	Nov. 18	-1-	Respiratory Disease 1 – Focus on Tests & Physiology (Yoshio Momose)
(20)	Nov. 18	-2-	Respiratory Disease 2 – Focus on Disease (Kazuo Hara)

Questionnaire on Baseline Medical Knowledge - Students in “Introduction to Clinical Medicine”



Graduate School of Medicine and Faculty of Medicine, University of Tokyo

Basic Medicine

- **Microbiology (Virus, Bacteria, Parasite, Infection Control)**
- **Anatomy (Macro, Histology)**
- **Immunology**
- **Physiology**
- **Biochemistry, Nutrition Science**
- **Pharmacology**
- **Hygiene**
- **Public Health**
- **Pathology**
- **Basics Integration Course**
- **Medical English**

*Figure removed due to copyright restrictions

Fig. DIRECT ANTI-ATHEROSCLEROTIC EFFECTS OF STATINS ON VASCULAR WALL. (ACROSS, March 2003)

Medicine, Medical Science

- Study of maintaining health through treatment/prevention of physical/mental illness
- Study with a clear objective of saving human lives
- Science dealing with lives born from human interactions

Healthcare, Medical Services/Practice

- Medical practice for patients
- Diagnosis, treatment, preventive examinations and health education

- Medicine based on experiments

Medicine is a collection of experiments.

-Claude Bernard

Helsinki Declaration

(Amendments: 1964, 2000, Additional Annotation: 2002)

(http://www.med.or.jp/wma/helsinki02_j.html)

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

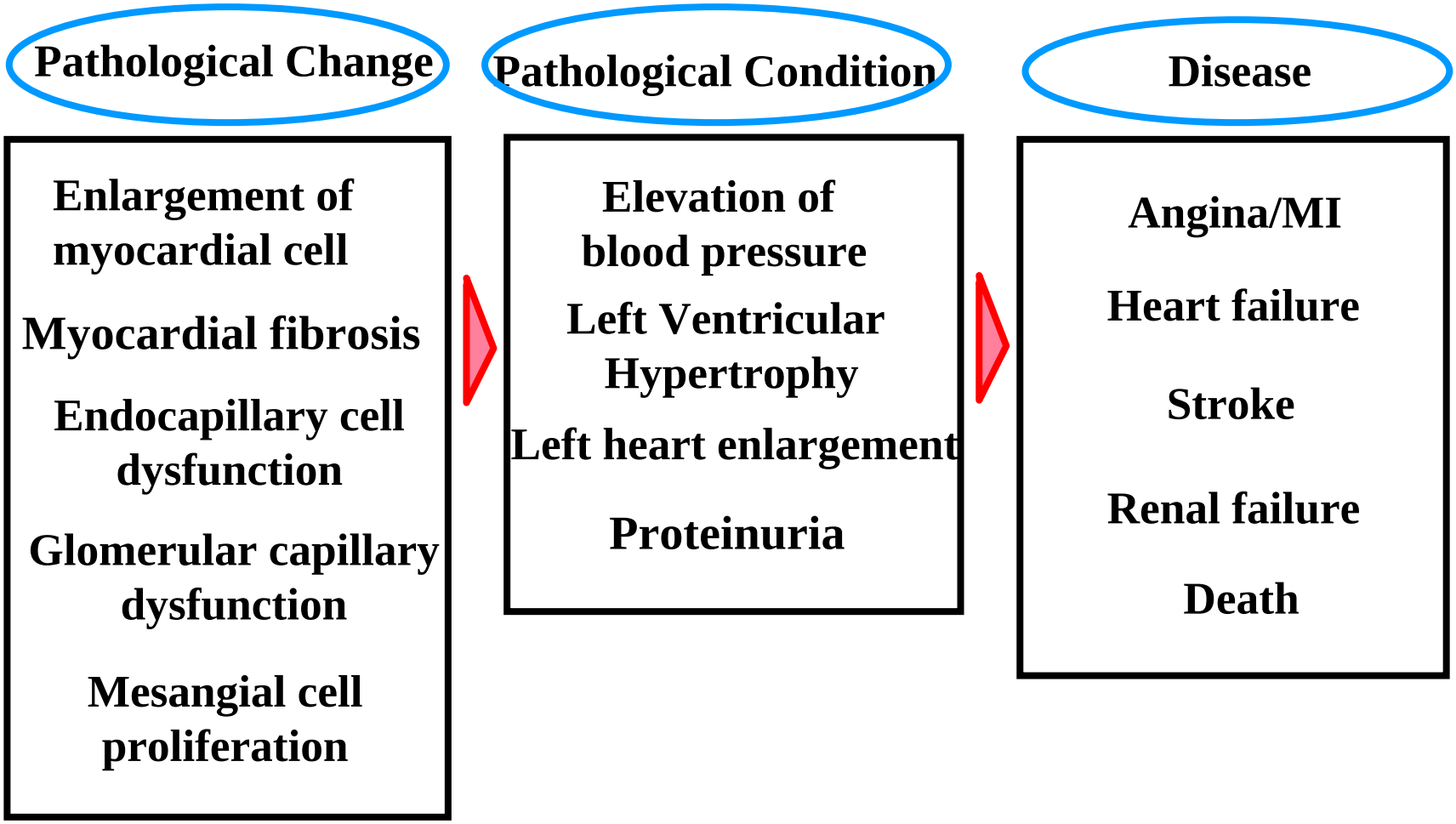
- Uncertainty in medicine

* **Acute illness**
  - **Infection**
  - **Trauma**
* **Chronic disease**
  - **Hypertension**
  - **Diabetes**
  - **Cancer**

- **Difference in duration of treatment time**
- **Difference in determination of therapeutic effect**

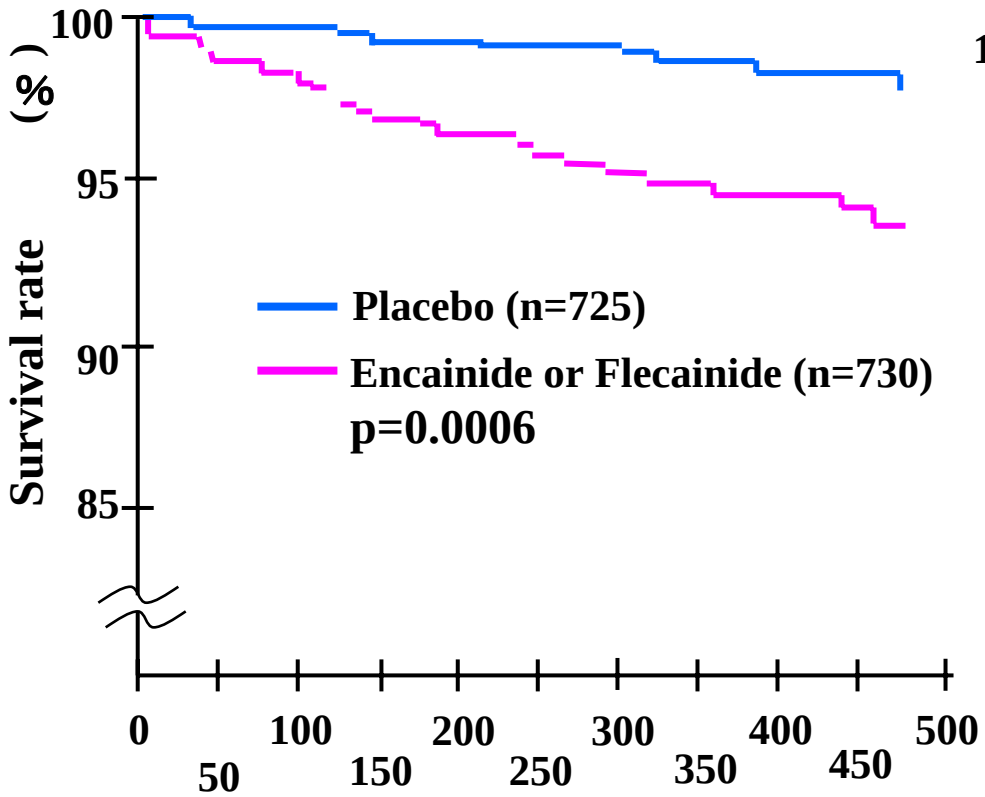
Hypertension

What should be considered in the evaluation of therapeutic effect?

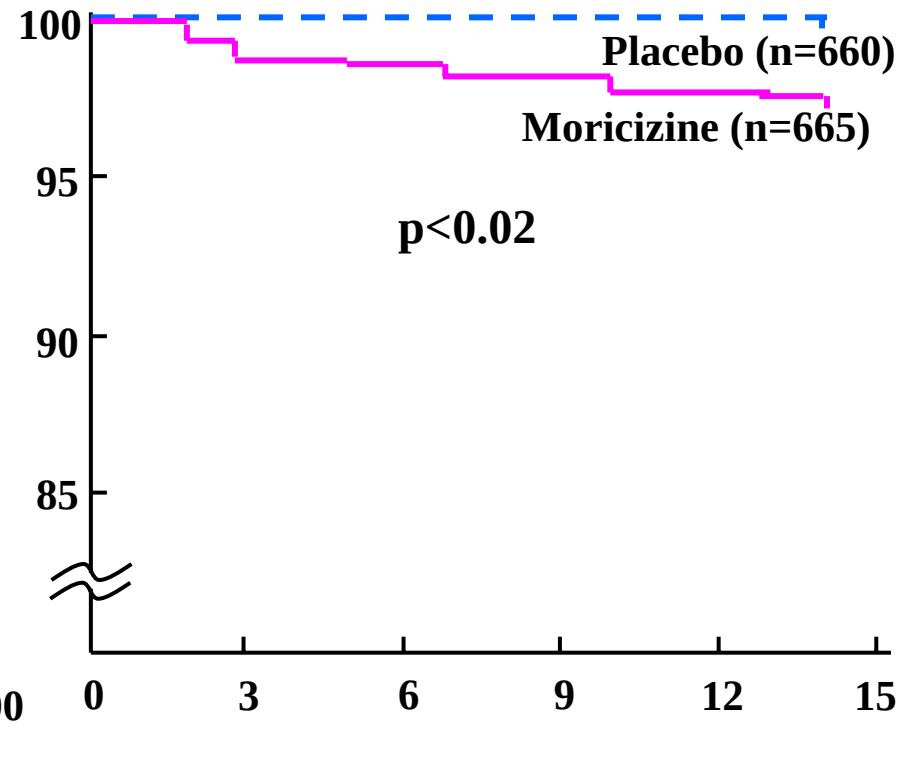


Examples of Discrepancy in Pathological Condition and Disease

Although "MI → arrhythmia → death" is predictable…



(N Engl J Med 1989, 321, 406-12)



(N Engl J Med 1992, 327, 227-33)

CAST: Cardiac Arrhythmia Suppression Trial

Discrepancy in Pathological Condition and Disease

Drug used (Test title)	Pathological condition	Result
Encainide & Flecainide (CAST)	Ventricular arrhythmia ↓	Sudden death ↑
Milrinone (Milrinone Test)	Hemodynamic improvement	Mortality rate ↑
Fibrate (WHO Fibrate Test)	Cholesterol ↓	Nonischemic disease mortality rate ↑
Isradipine (MIDAS)	Anti-arteriosclerotic	Cardiovascular disease occurrence ↑

In the end, it has to be tested on humans…

ML-236B, a precursor of Mevalotin, showed no effect on rats.

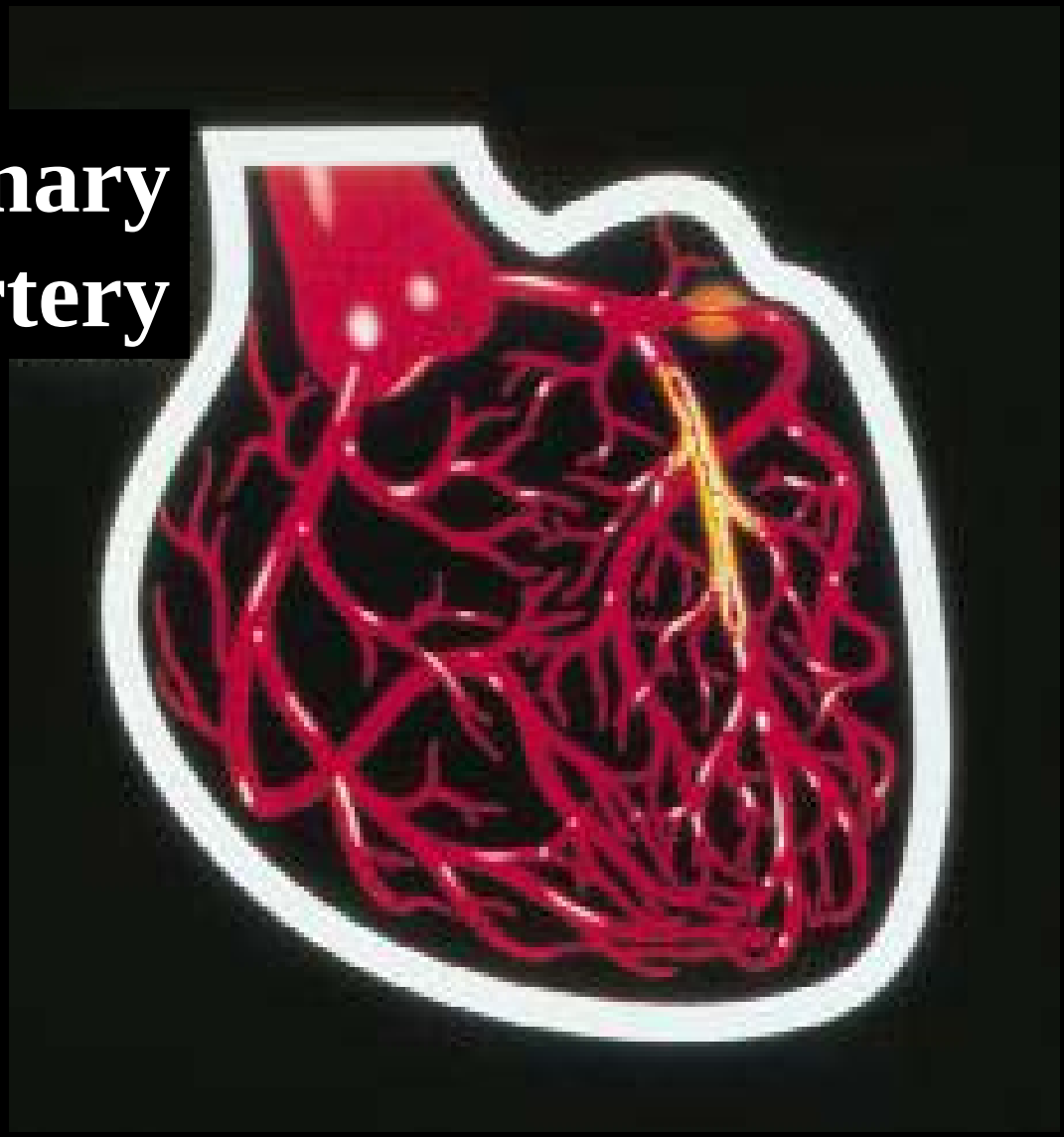
↓

It showed a dramatic hypocholesterolemic effect on a retiring hen.

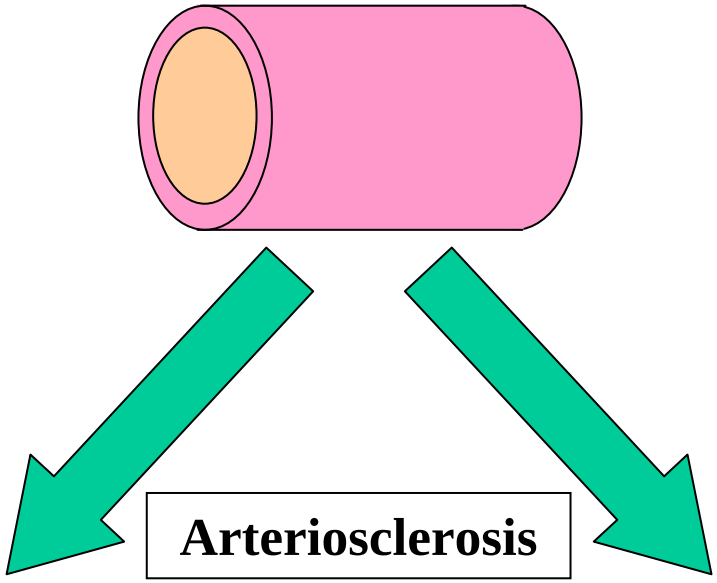
↓

When given to a dog, a trace of metabolite appeared in the urine showed a stronger hypocholesterolemic effect than ML-236B itself. Mevalotin was developed from this metabolite.

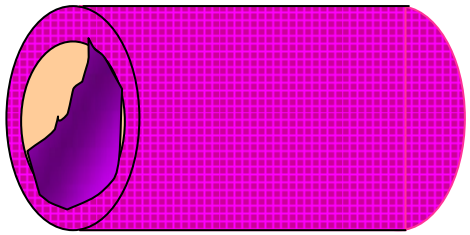
Coronary Artery



Normal Coronary Artery

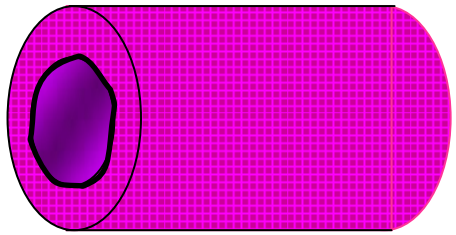


Angina



Heart muscle is recoverable.
Pumping function →

MI



Heart muscle dies.
Pumping function ↓

Treatment of Angina/MI

- Improvement of the heart's blood supply
(Revascularization)

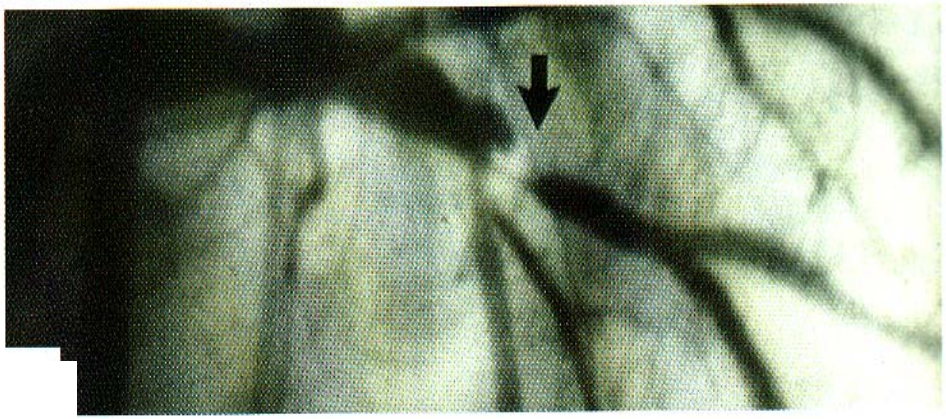
Invasive medical therapy (Angioplasty)

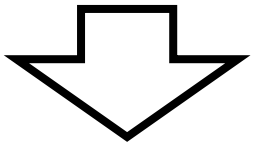
Surgical therapy (Bypass surgery)

- Drug therapy

- Improvement of life style

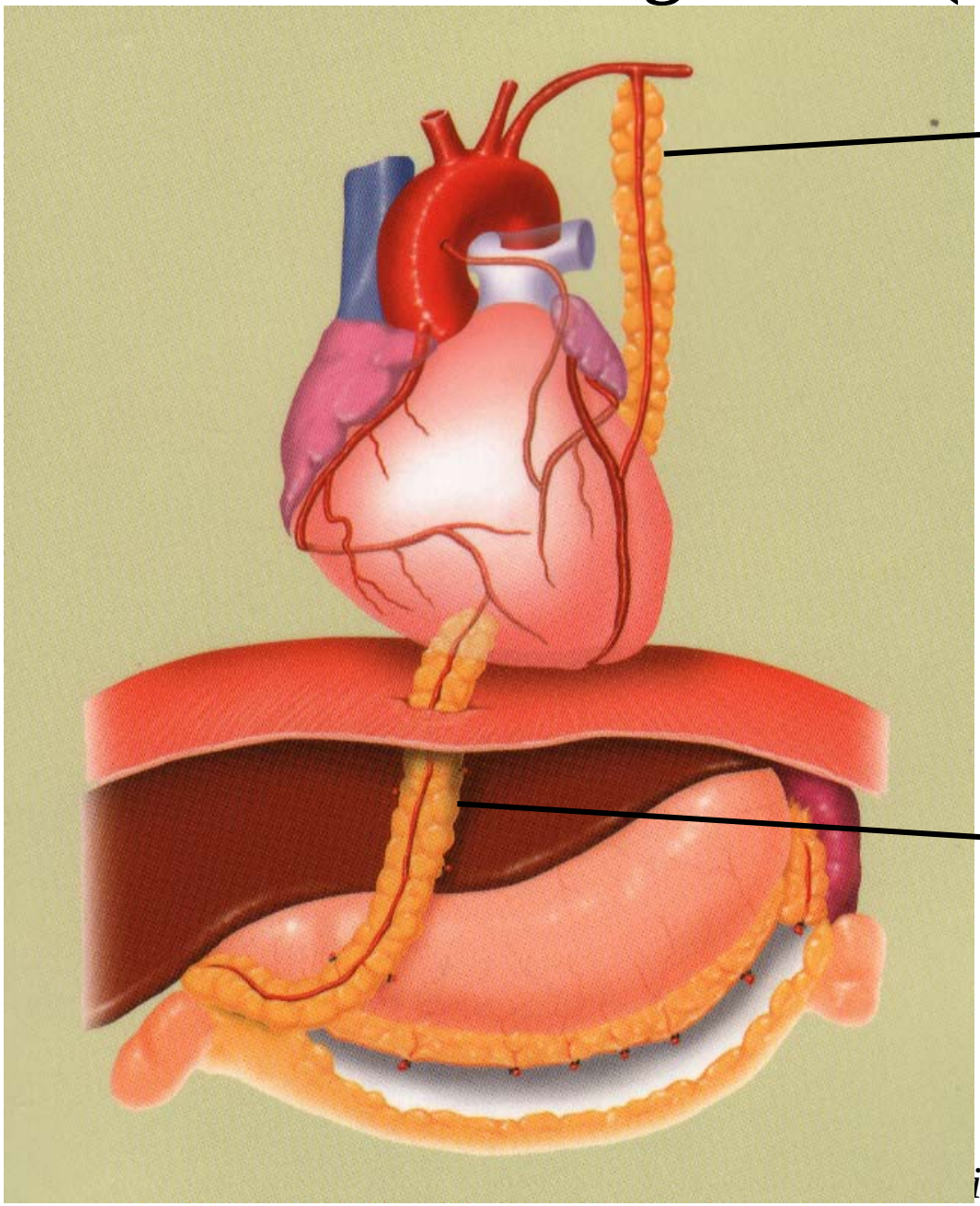
Treatment of Angina/MI (Invasive Medical Therapy)





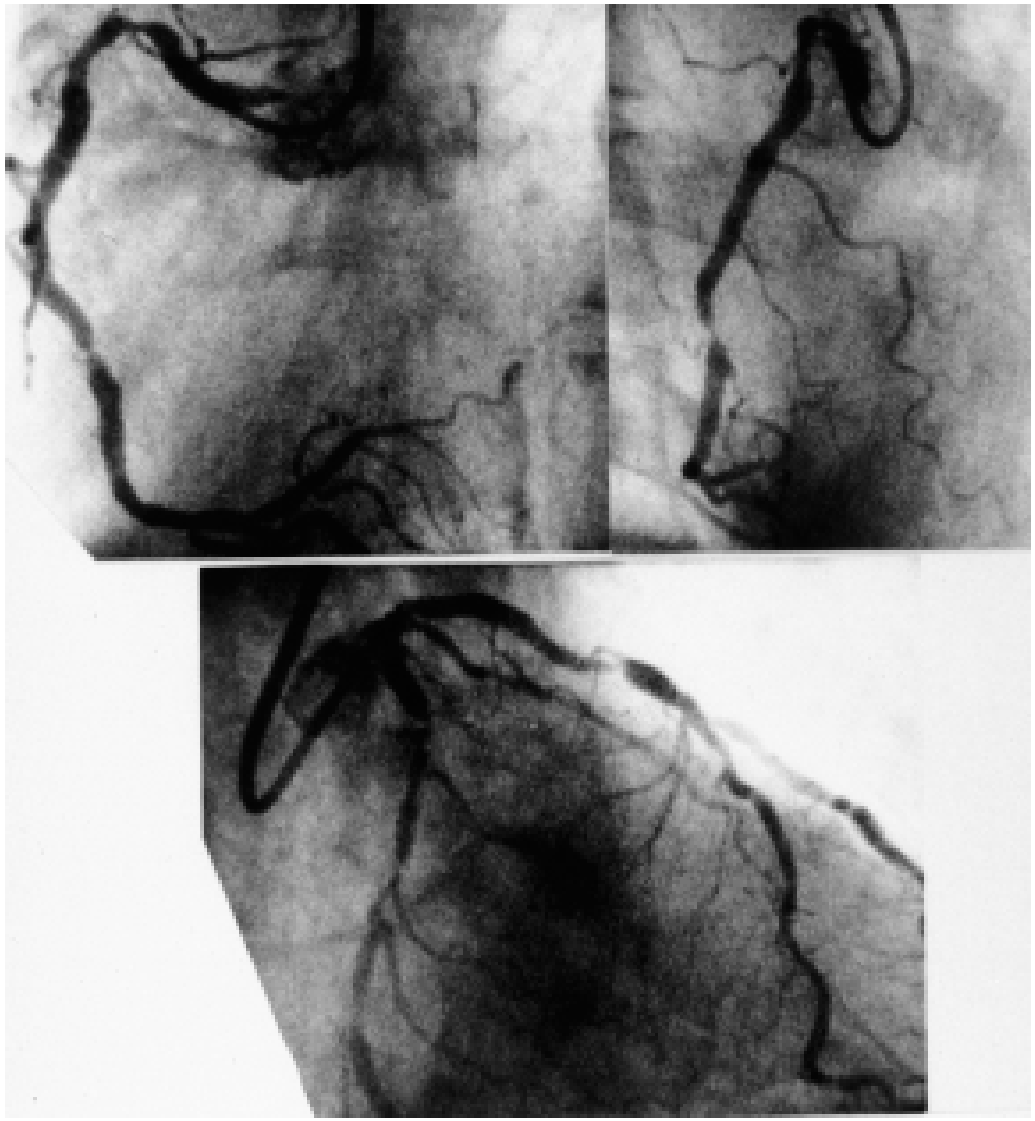
- **Expand with a balloon.**
- **Place a stent (metallic mesh) to hold the artery open.**
- **Remove with a drill.**
- **(Radiation)**

Treatment of Angina/MI (Surgical Therapy)

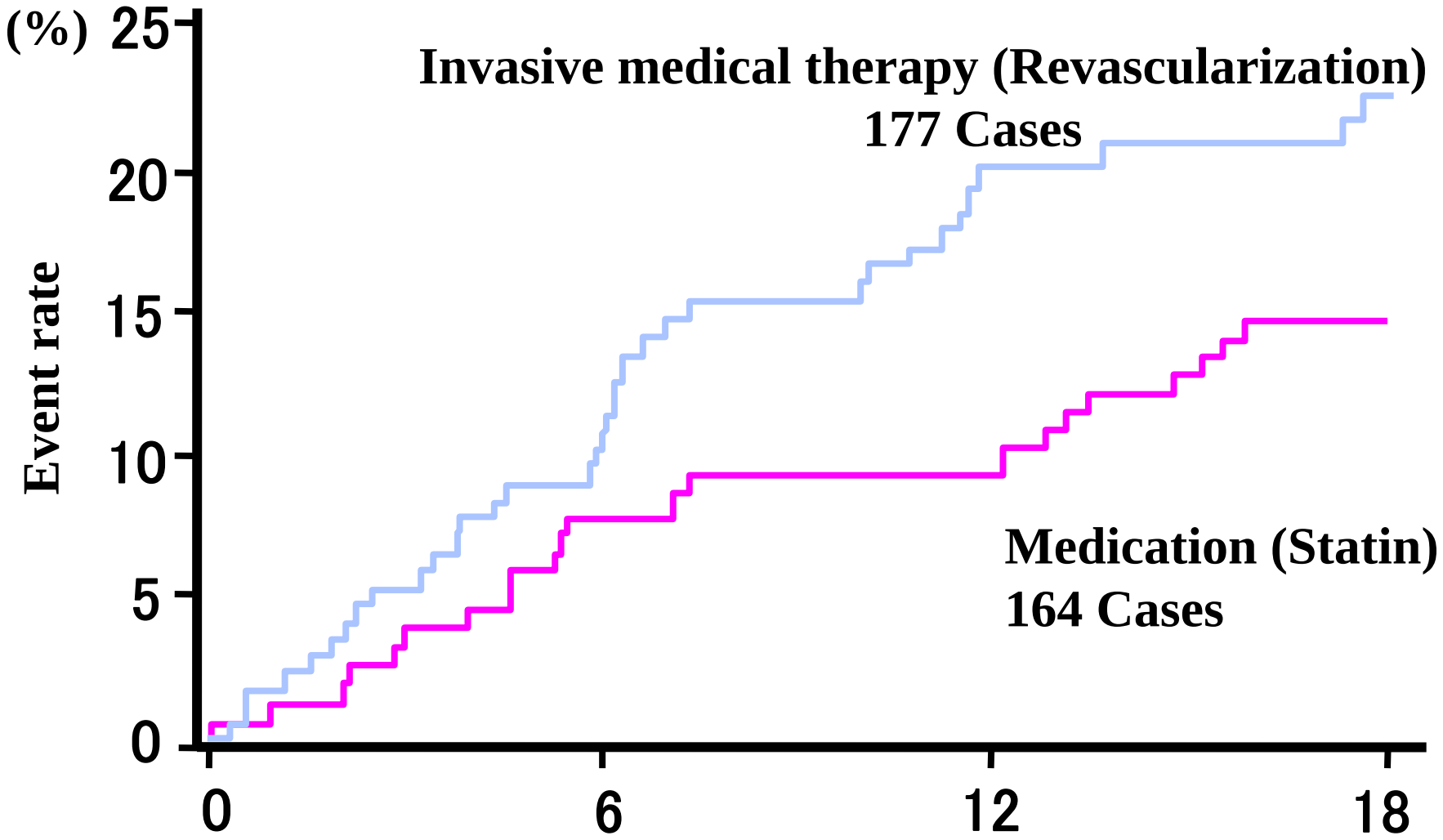


Internal mammary artery graft

Gastroepiploic artery graft

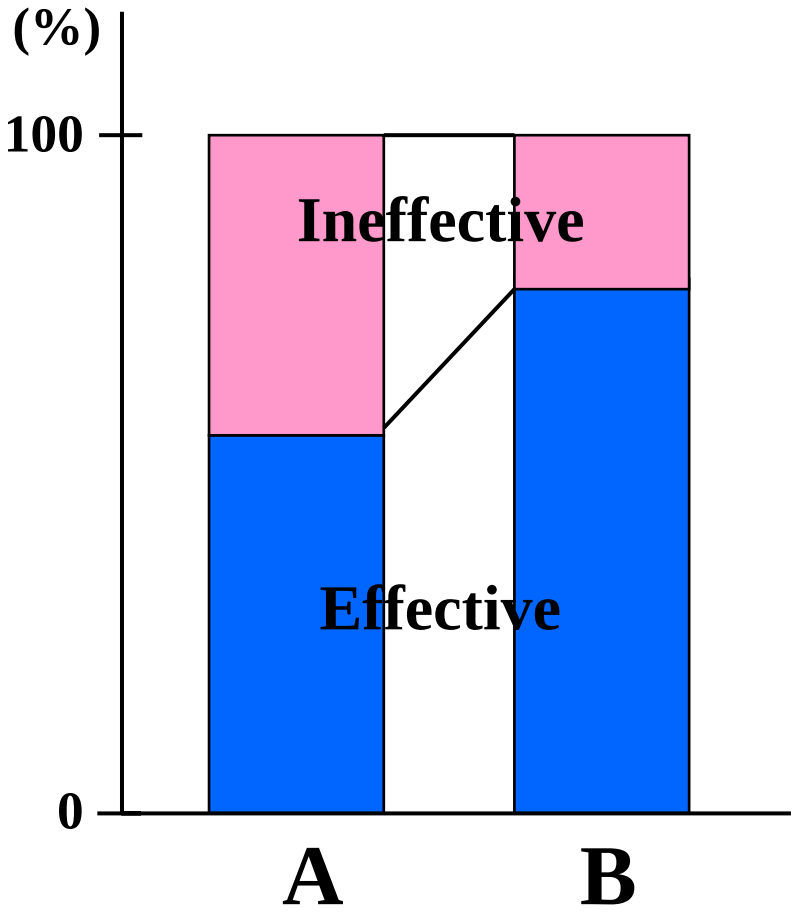


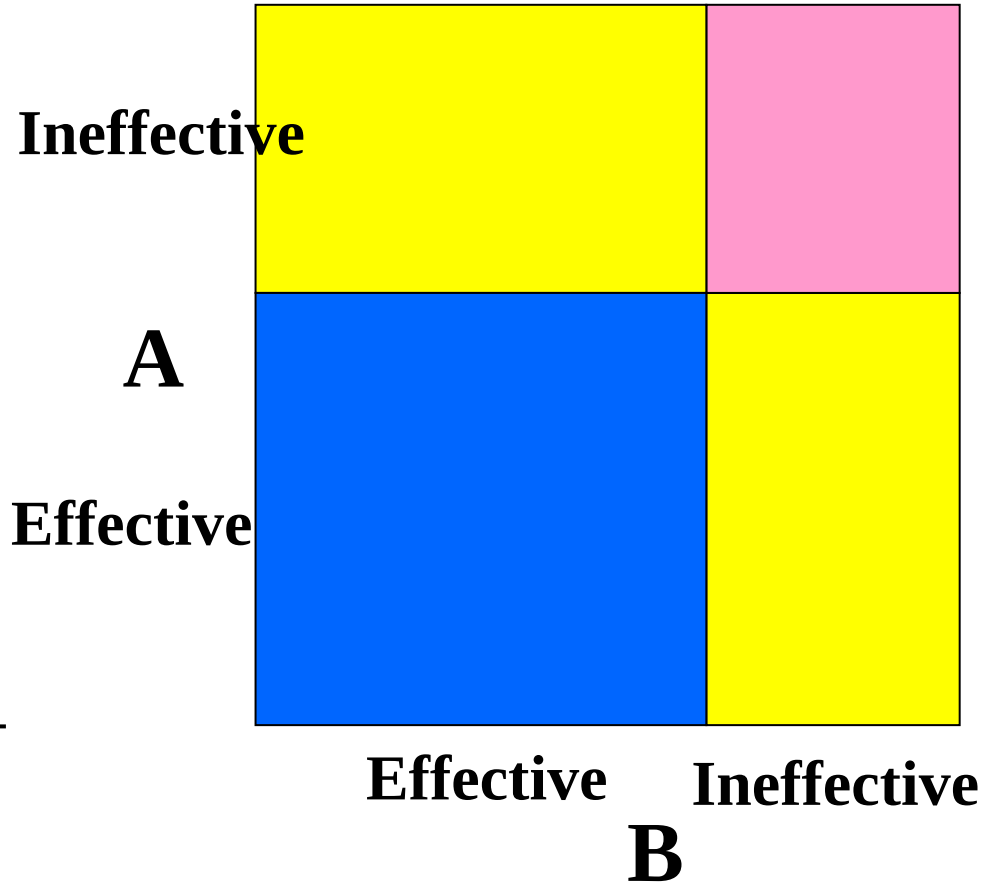
Ischemic Event Rate in Stable Angina



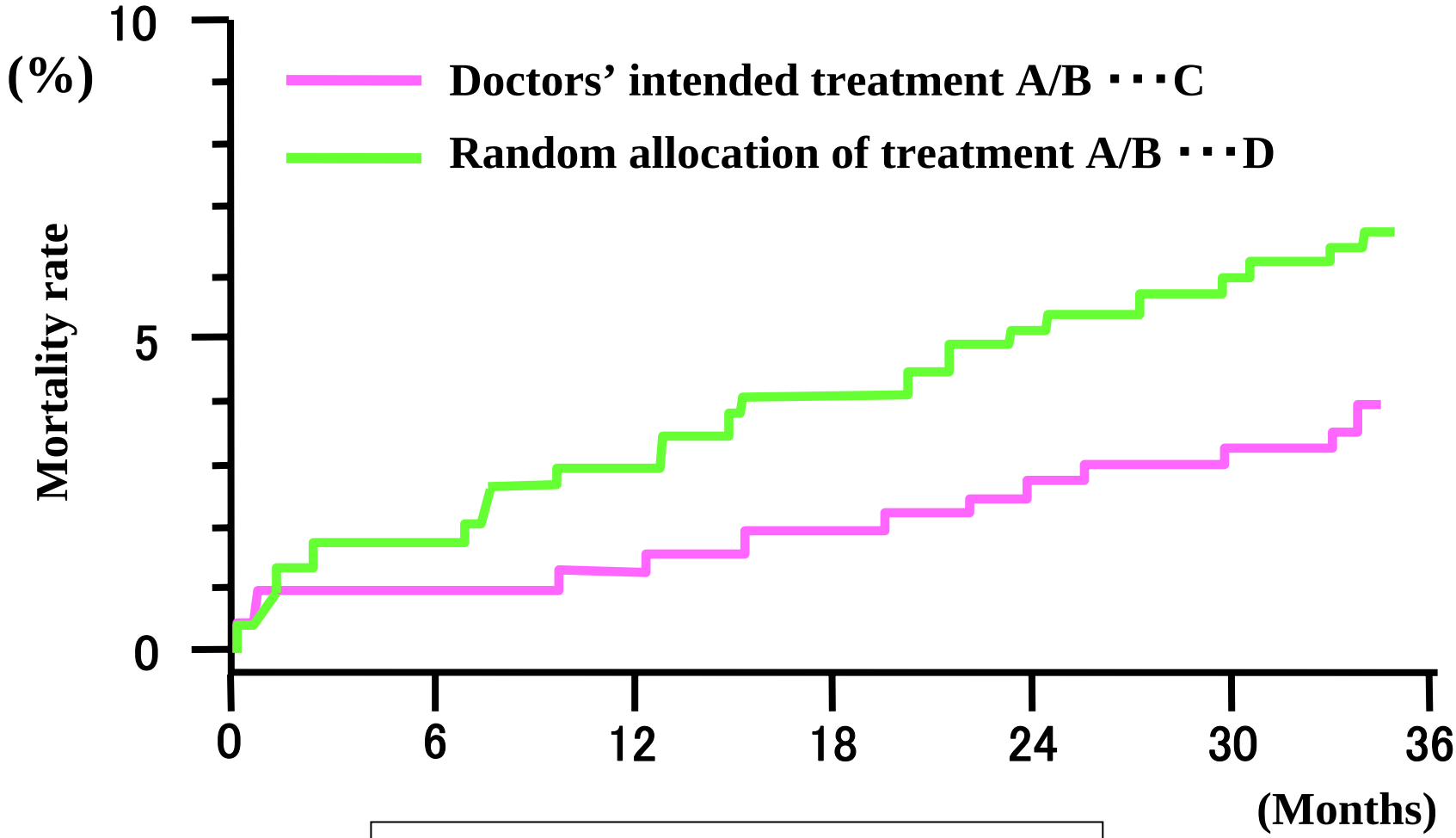
(Pitt B *et al* N Engl J Med 1999, 41, 70-76)

Is treatment B better? -Not always.





Difference in Therapeutic Effect – Random Allocation and Intended Treatment



The result: C>B>D>A

(Am J Cardiol 1997, 79, 1453)

Different Cause of Illness

Pathogen
Harmful substance
Accident
Stress
etc.

Environmental Factors

Genetic Factors

Genetic predisposition
Aging
etc.

Illness

Life Style Factors

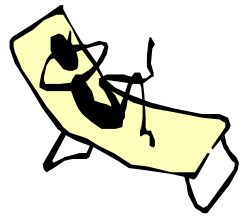
Diet

Exercise

Smoking

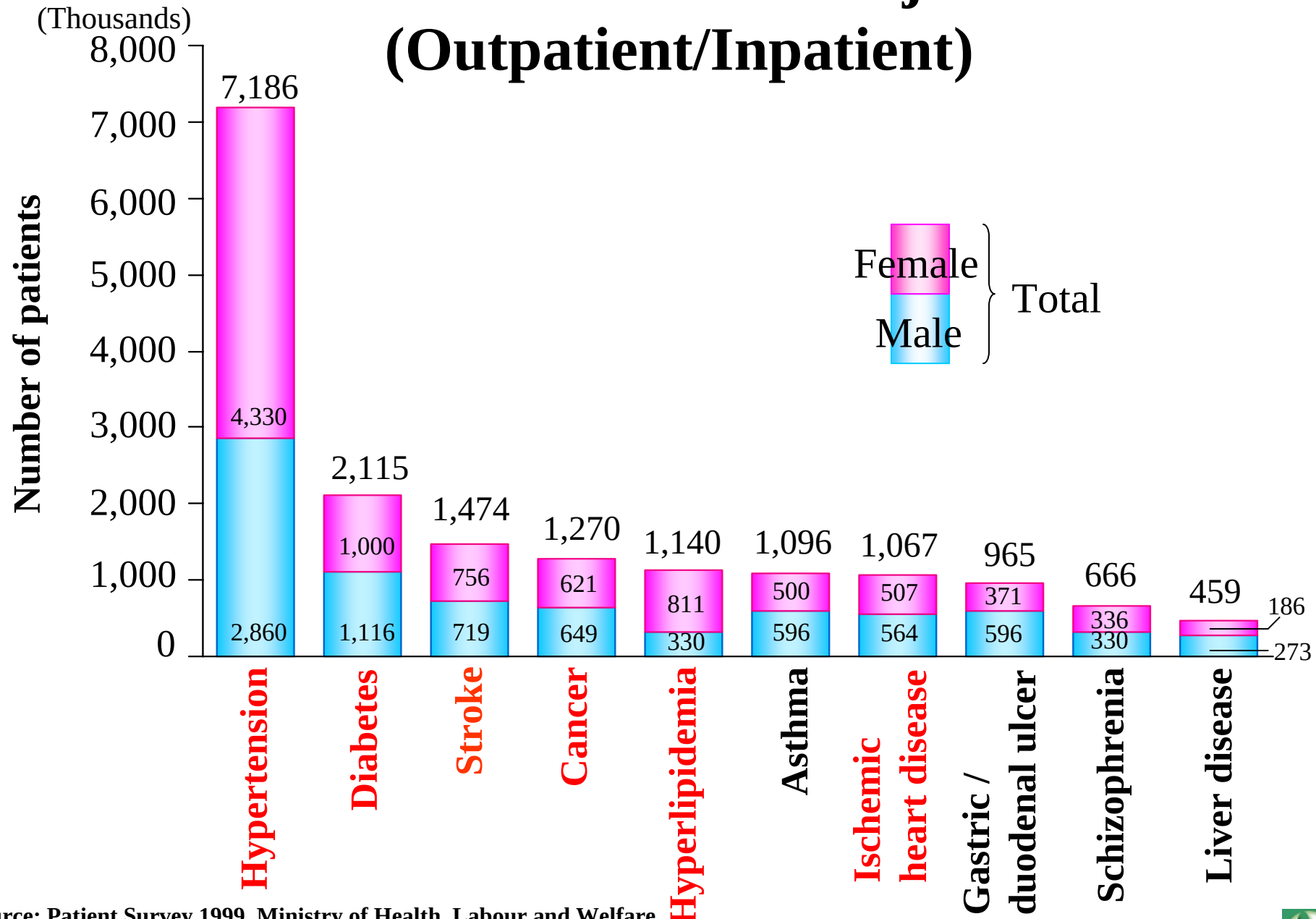
Alcohol

Rest



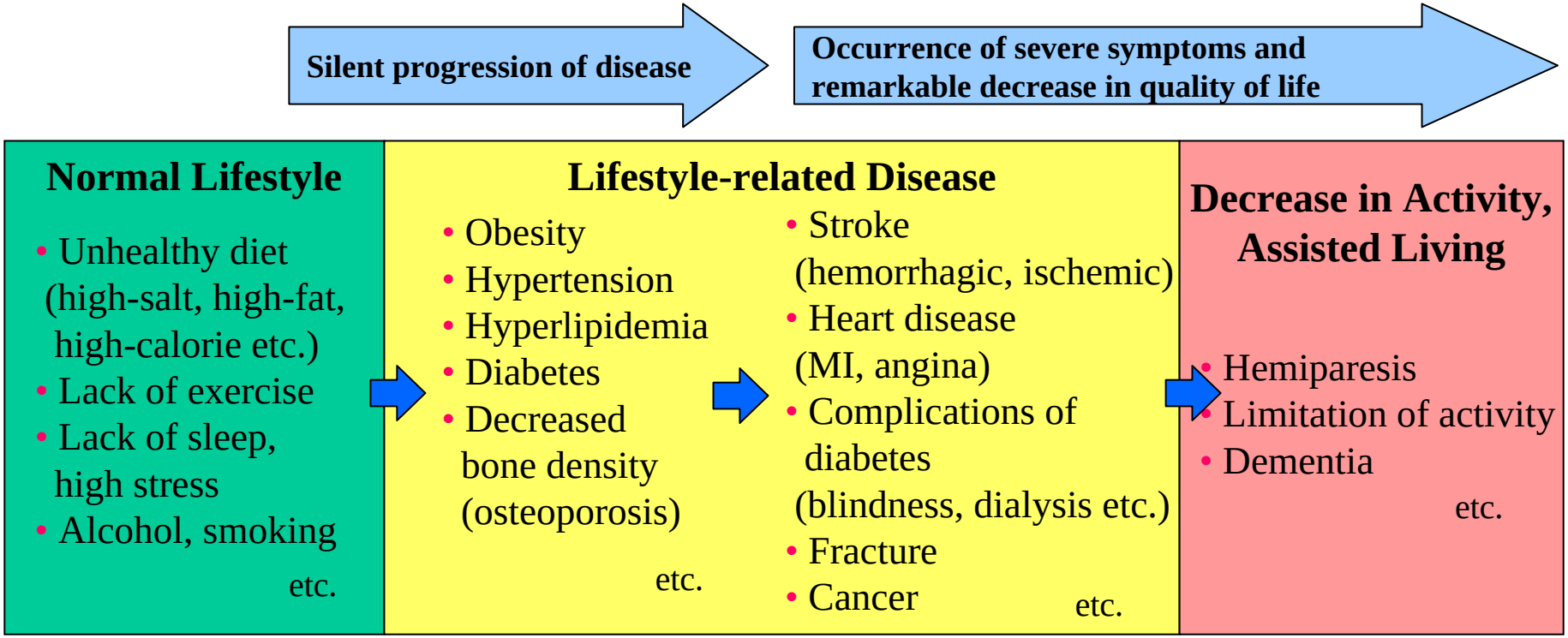
etc.

Number of Patients with Major Disease (Outpatient/Inpatient)



Source: Patient Survey 1999, Ministry of Health, Labour and Welfare

Progression of Lifestyle-related Disease & Its Relation to Primary/Secondary/Tertiary Prevention



[Primary Prevention] **[Secondary Prevention]** **[Tertiary Prevention]**

Preventive Medicine **Therapeutic Medicine, Rehabilitation**

Objective of Medicine/Healthcare

Sanctity of life (SOL)

Quality of life (QOL)

Physical

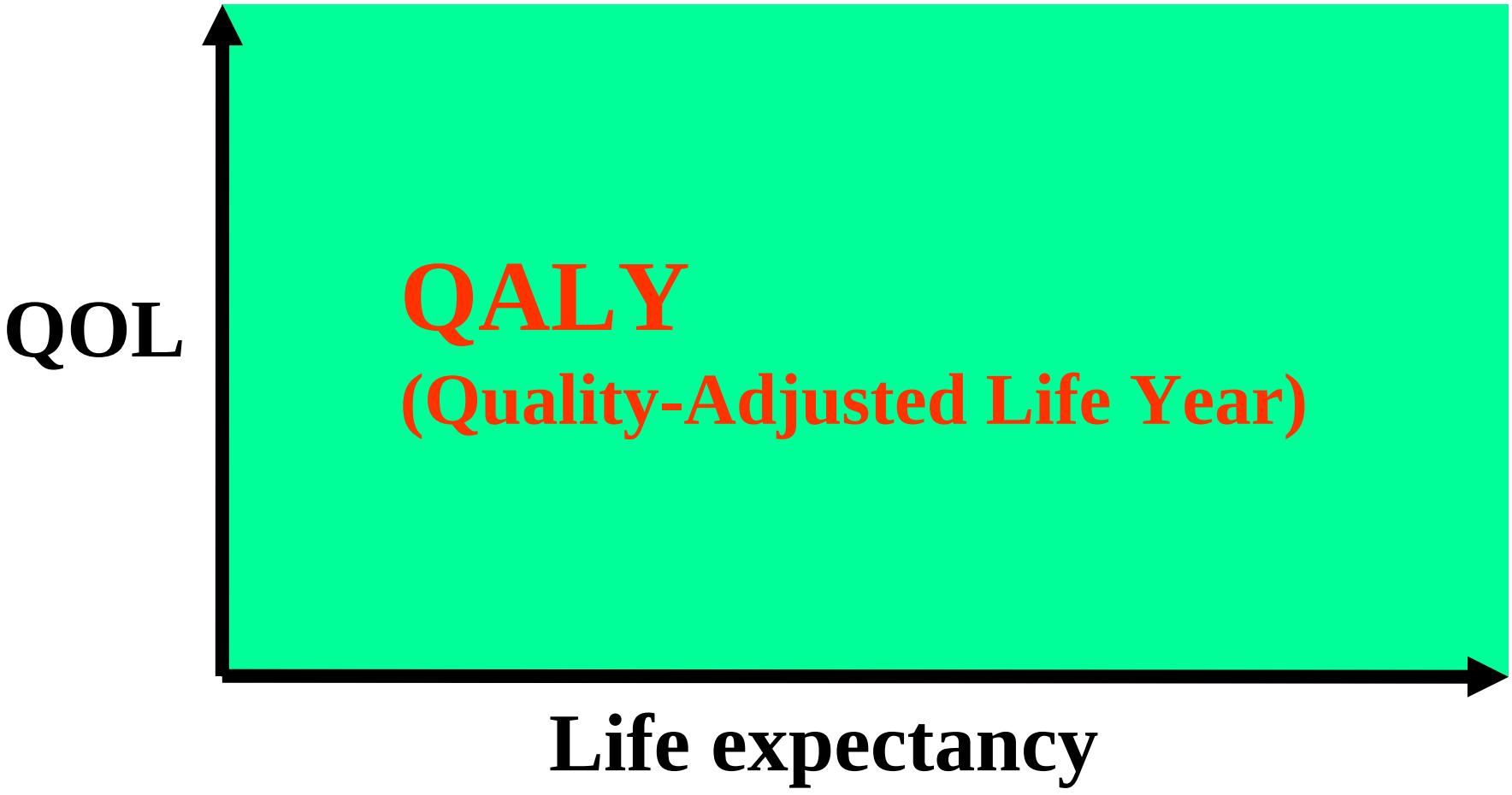
Psychological

Healthy Life Expectancy

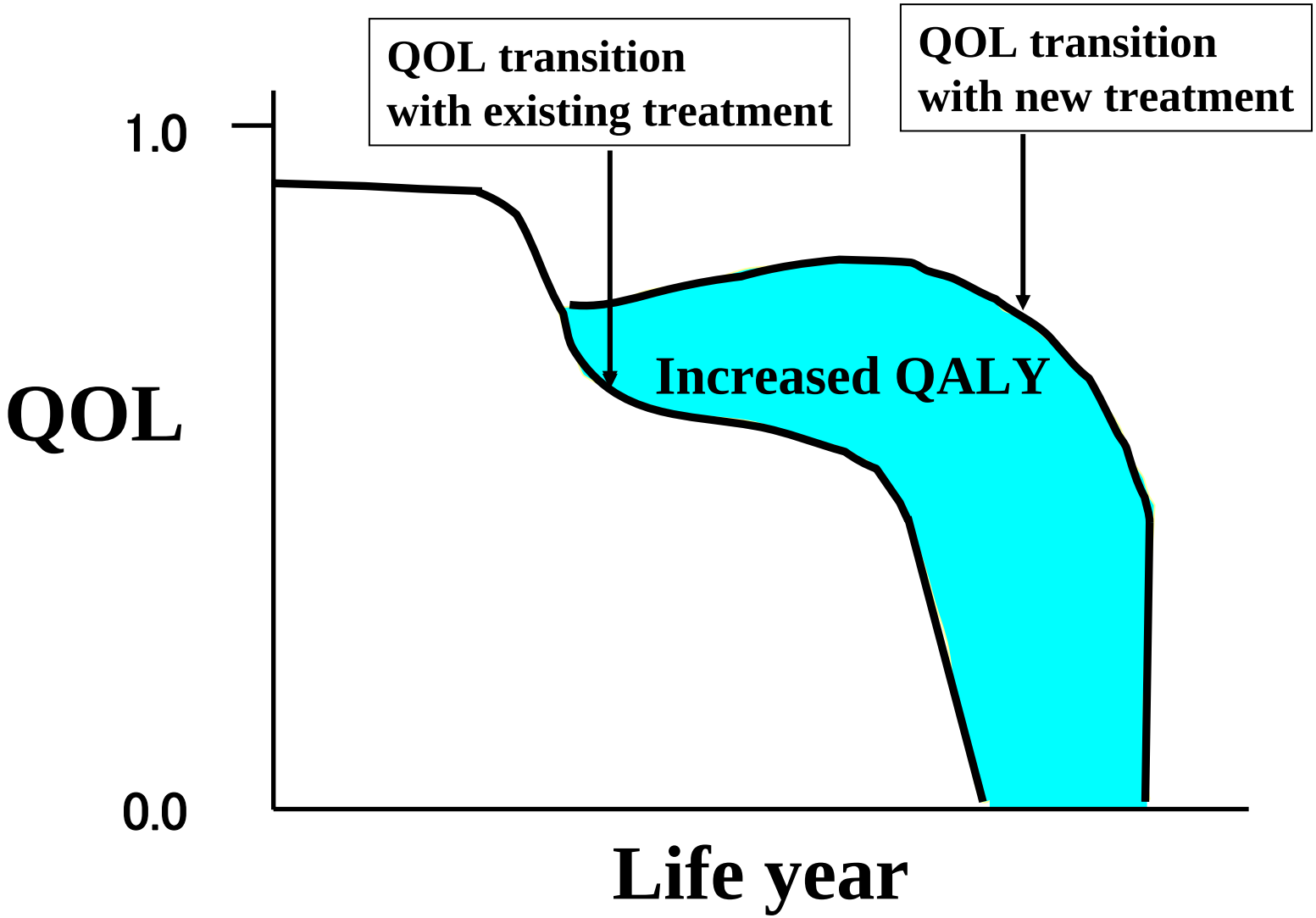
→Life span with which one is maintaining QOL

For example, one year decrease in (Life Expectancy) - (Healthy Life Expectancy) results in estimated three trillion yen reduction of healthcare cost.

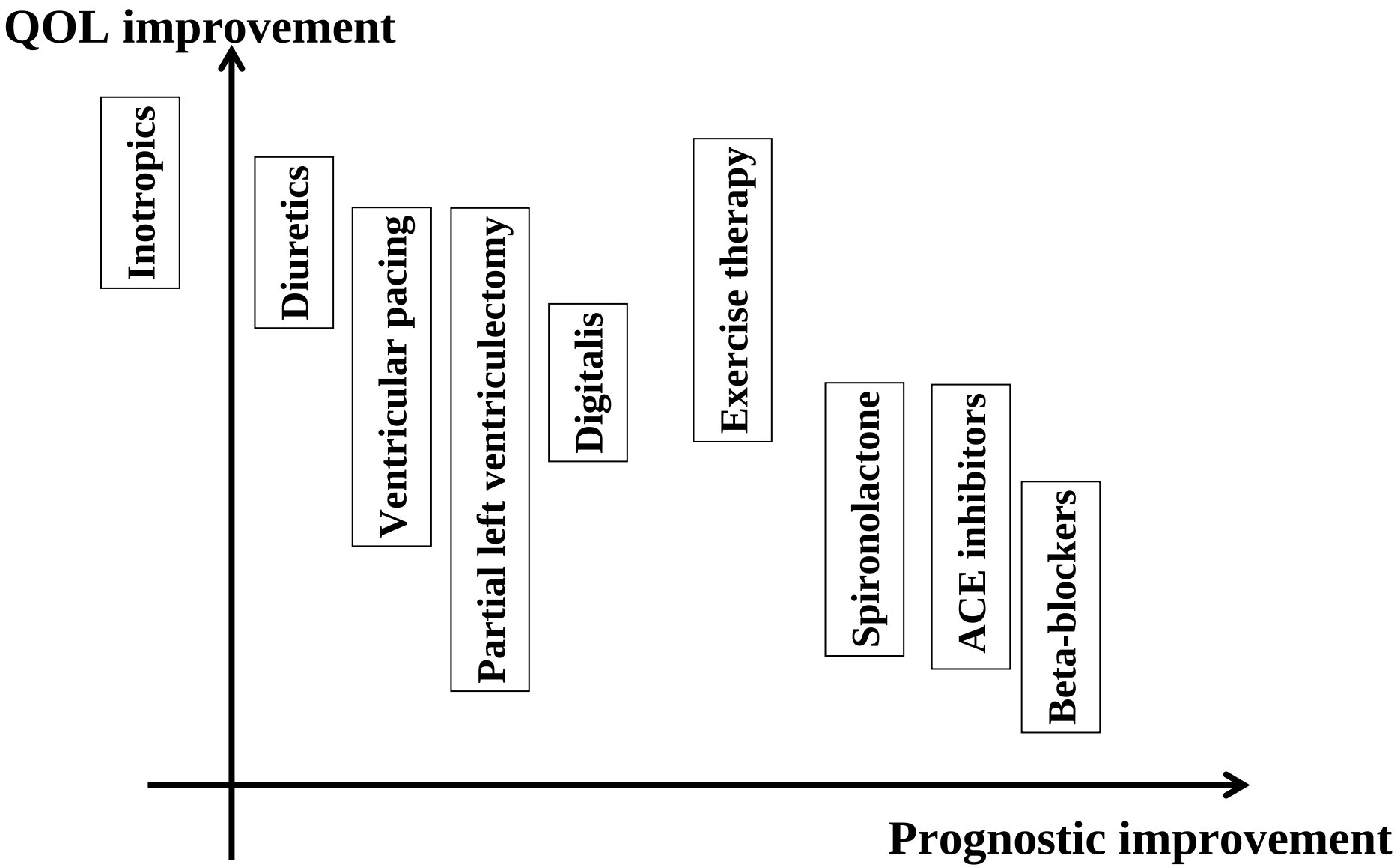
Improvement of QOL & Life Expectancy



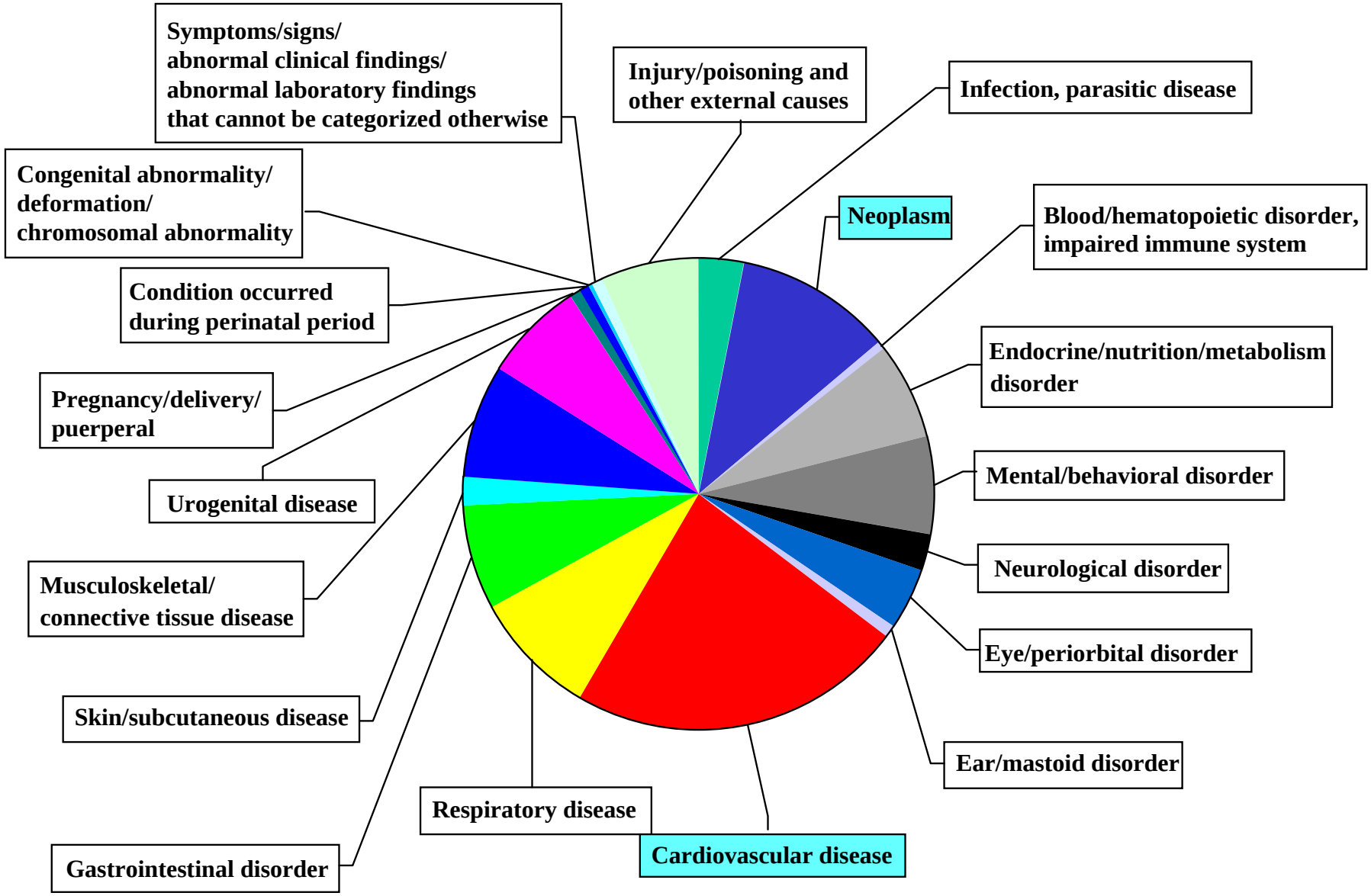
Treatment to Increase QALY



Prognostic Improvement and QOL Improvement of Different Heart Failure Treatments



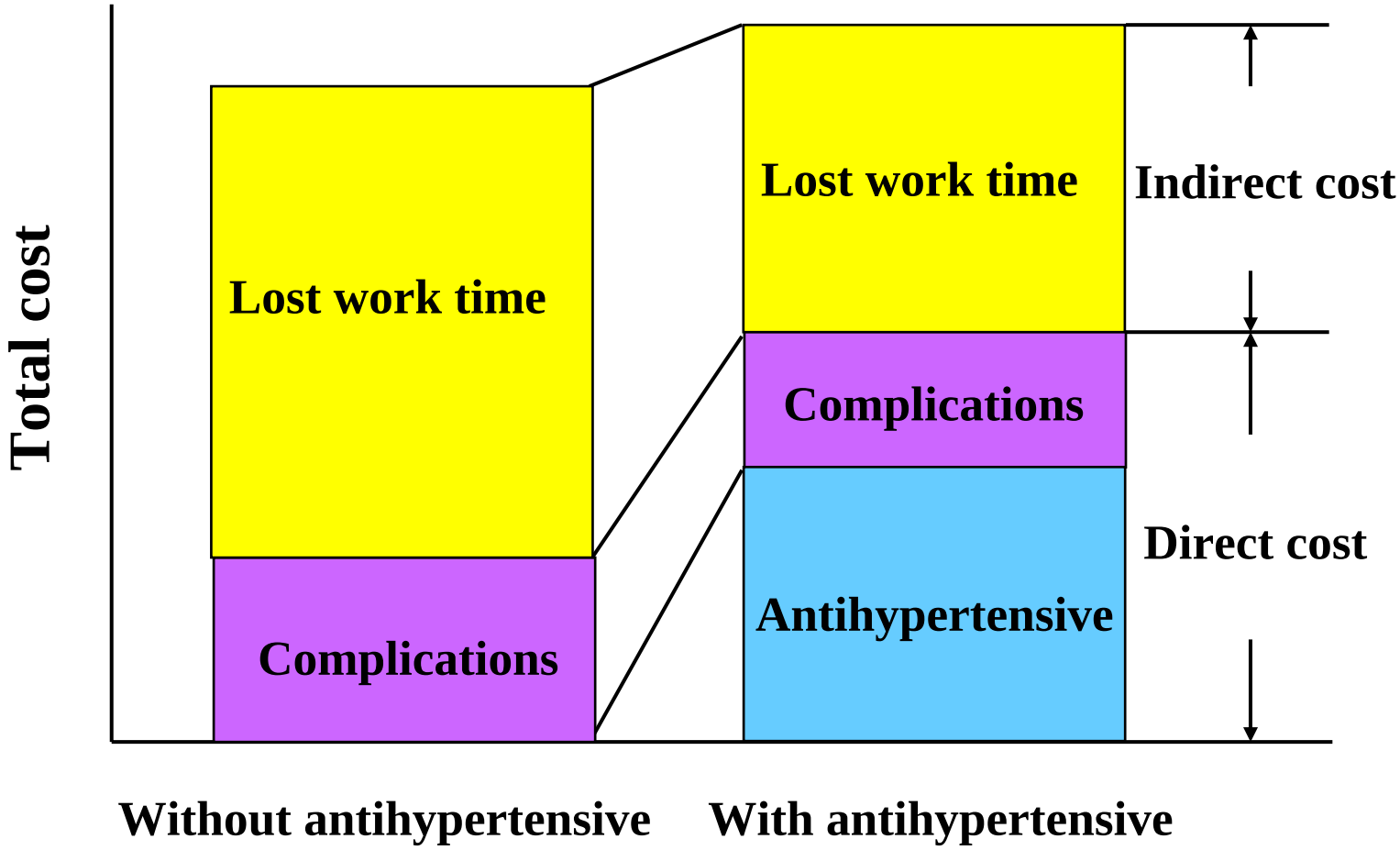
Breakdown of General Healthcare Costs (FY1999)



http://www.mhlw.go.jp

Source: National Healthcare Cost Review, excerpt from MHLW website

Cost of Illness
Patient with Hypertension



Medication Cost for Preventing one Incident of MI, Stroke or Death in Mild/Moderate Hypertension Patient without Complications (USD)

Medication	Middle age	Old age
Diuretics	4,730 (1)	1,595 (1)
Beta-blockers	54,782 (12) - 105,092 (22)	18,473 (12) - 35,438 (22)
ACE inhibitors	94,170 (20) - 156,520 (33)	31,755 (20) - 52,780 (33)
Alpha-blockers	151,188 (32) - 194,360 (41)	50,982 (32) - 65,540 (41)
Calcium antagonists	128,570 (27) - 346,236 (73)	43,355 (27) -116,754 (73)

(Modification of Pearce KA *et al* Am J Hypertens 1998,11,618)

Common Side Effects of Antihypertensive

Diuretics	**electrolyte abnormality, hyperlipidemia, impaired glucose tolerance, hyperuricemia, hemoconcentration, erectile dysfunction etc.**
Beta-blockers	**bradycardia, atrioventricular block, peripheral circulatory disturbance, asthma, fatigue, less tolerance for physical activity etc.**
ACE inhibitors	**hacking, dyspnea caused by angioneurotic edema (rare)**
Alpha-blockers	**orthostatic hypotension, postprandial hypoglycemic action**
Calcium antagonists	**facial flushing, headache, palpitation, extremity edema, constipation, gingival hypertrophy**

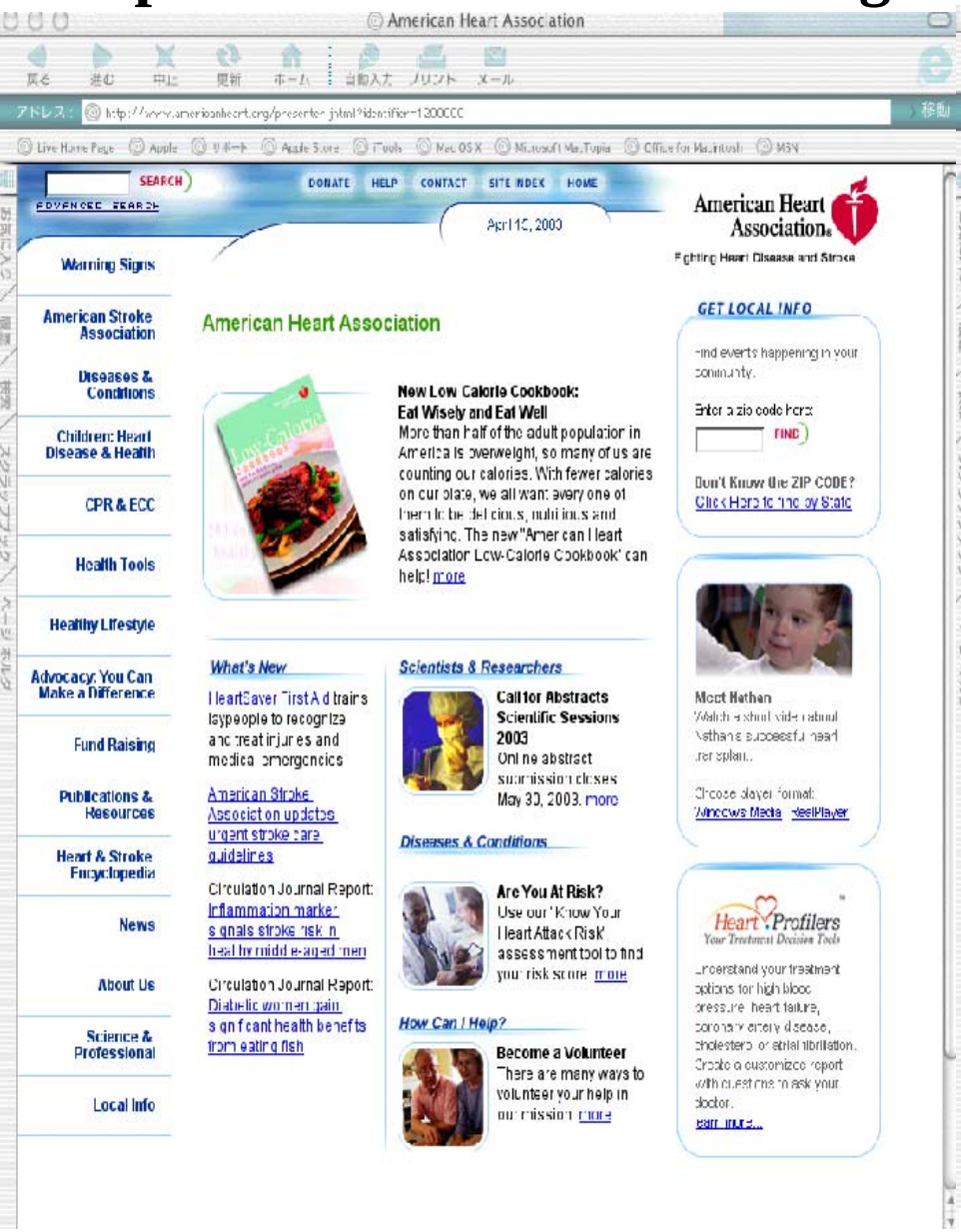
Asymmetric Information

［Healthcare Providers (Producer)＞＞Patients (Consumer)］

Public regulations have been enacted for consumer protection and financial stability.

The asymmetry should be corrected in the future.

< American Heart Association >
http://www.americanheart.org



< Japanese Circulation Society >
http://www.j-circ.or.jp