



DIAGNOSTICS: THE CORNERSTONE OF COMPREHENSIVE PATIENT CARE

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Role of the Lab

- **Central role in healthcare**
- **70% of all medical decisions based on lab results**
- **In the US cost of lab only 3.5% of total healthcare dollars**
- **High clinical value at relatively low cost**



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Purpose and Function of Clinical Laboratory

- **Confirm or reject a diagnosis**
- **Establish prognosis**
- **Guide patient management**
- **Monitor efficacy of therapy**
- **Screen for diseases**
- **Provide guidelines for test utilization**
- **Detect predisposition to disease**



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Reliable result in appropriate
time at affordable price



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Types of Laboratory Models

- **Traditional hospital lab**
- **Stand- alone lab**
- **Core labs: chematology (chemistry + hematology)**
- **Regional lab: low volume esoteric tests**
- **Reference Lab: Traditional full service lab for all types of testing especially esoteric tests**
- **Point of Care testing: lab at patients bedside**
- **Stat lab in emergency room/OT for blood gases and hematocrits**



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Optimizing Performance

- **Operations management**
- **Human resource management**
- **Financial management**
- **Marketing management**



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Disciplines in Lab Medicine

- **Biochemistry**
- **Hematology**
- **Microbiology**
- **Clinical pathology**
- **Histopathology**
- **Cytology**
- **Immunohistochemistry**
- **Immunofluorescence**
- **Immunopathology**
- **Oncology**
- **Endocrinology**
- **Genetics**
- **Nutrition & metabolism**
- **Toxicology**



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High Ended Esoteric Tests

➤ **Molecular Diagnostics**

➤ **Flowcytometry**

➤ **Cytogenetics**

➤ **Biochemical genetics**

➤ **Biophysics:**

- FTIR (Fourier Transform I–R Spect)
- Atomic Absorption Spectrometry



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Good Laboratory Practices

- **Ordering the right test**
- **Proper collection and transportation of sample**
- **Receipt & distribution of sample**
- **Sample processing**
- **Testing of sample**
- **Review of results**
- **Release result after rechecking and clinical correlation**
- **Reporting of results**



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Specimen Collection and Handling

Institution of specific phlebotomy policies & procedures are necessary to avoid pre-analytical errors with special attention to:

- patient conditions for sample collection
- standardized of sample containers
- correct volume of blood
- bar coding: identifies patient and tests



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Sample Testing

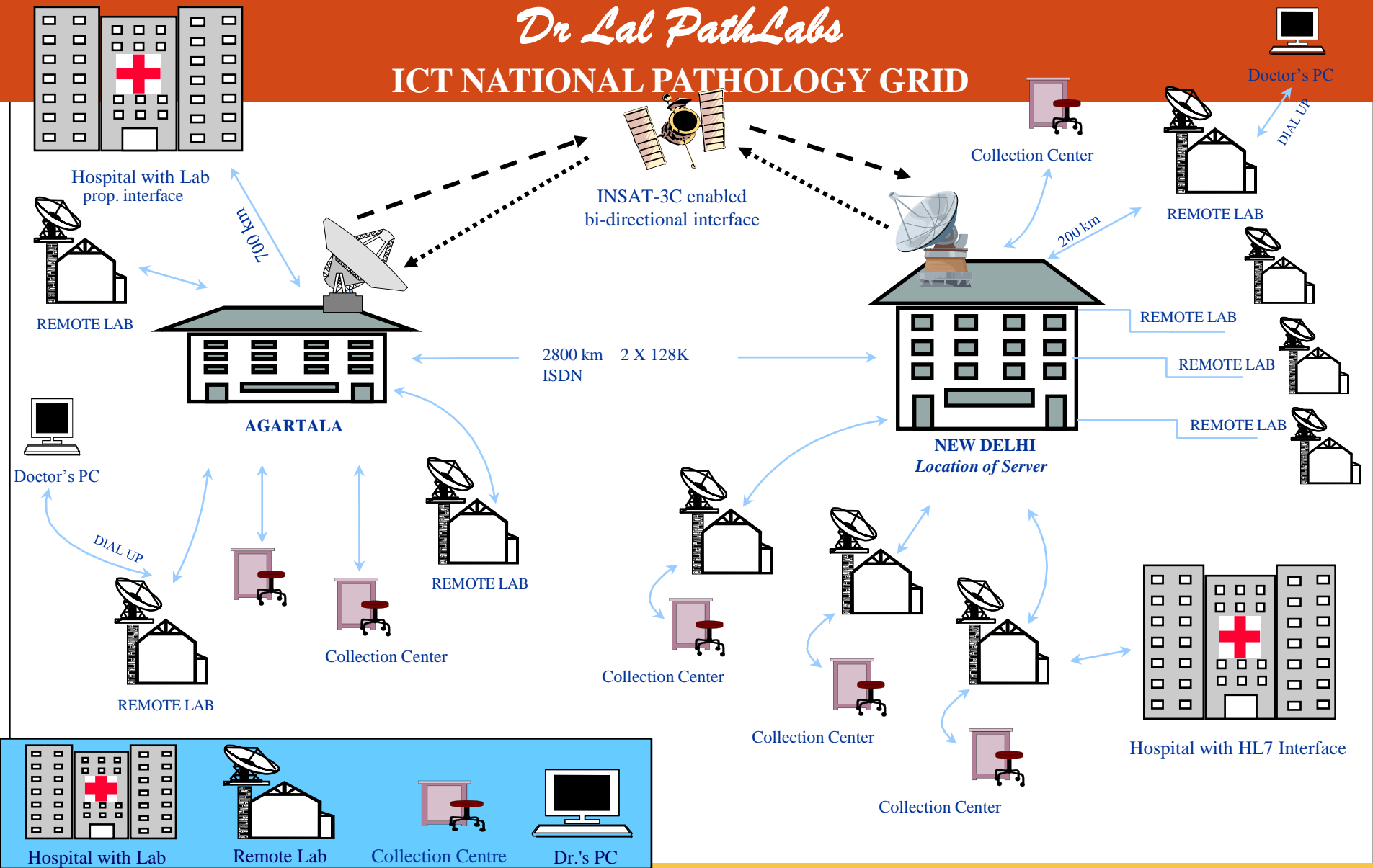
Technology is a means to an end, not an end in itself

- **Automation:** accuracy, precision, speed
 - primary tube with bar code
 - robotics
 - bi-directional interface**
- **Strict adherence to Quality control protocols**
- **Proficiency testing**



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ICT NATIONAL PATHOLOGY GRID



Reporting

- **Bi-directional interface; no transcription errors**
- **Validation of results by competent staff**
- **Rechecking of abnormal values**
- **Discussion of lab results with clinician**
- **Availability of results on-line**



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Interpretation of Results

- Does an abnormal result truly reflect disease & does a normal result necessarily indicate a disease free state?
- Never rely on a single value to make a diagnosis

Factors to be considered:

- Reference Range for the population
- Pre-analytical variables
- Analytical error
- Biological variability
- Sensitivity and specificity of the assay
- Clinical correlation



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How diagnostics can change the future of healthcare?

- **Diagnostics can enable a more efficient and effective healthcare system**
- **Power of diagnostics to change the focus of healthcare from treating sickness to promoting wellness**
- **Personalized medicine – A reality today through molecular diagnostics**

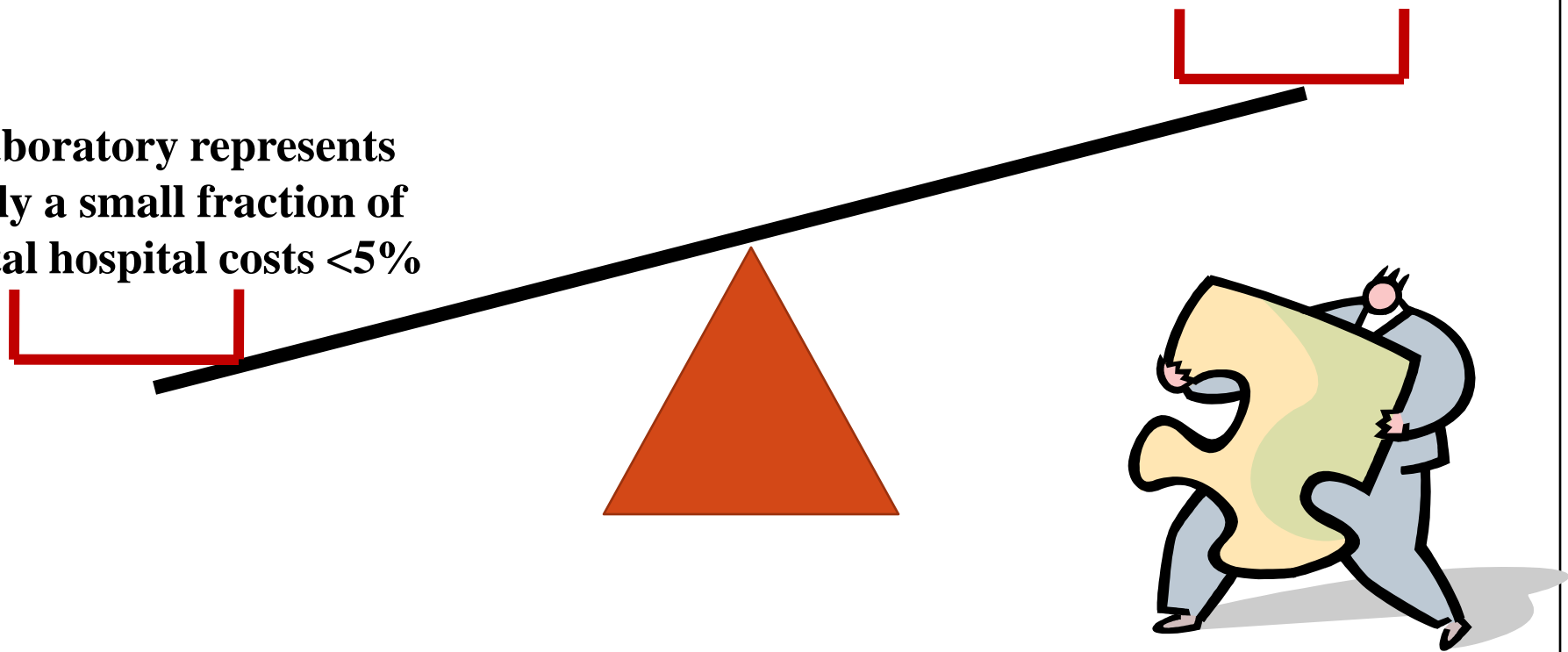


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Laboratory Medicine: A cornerstone for modern health systems!

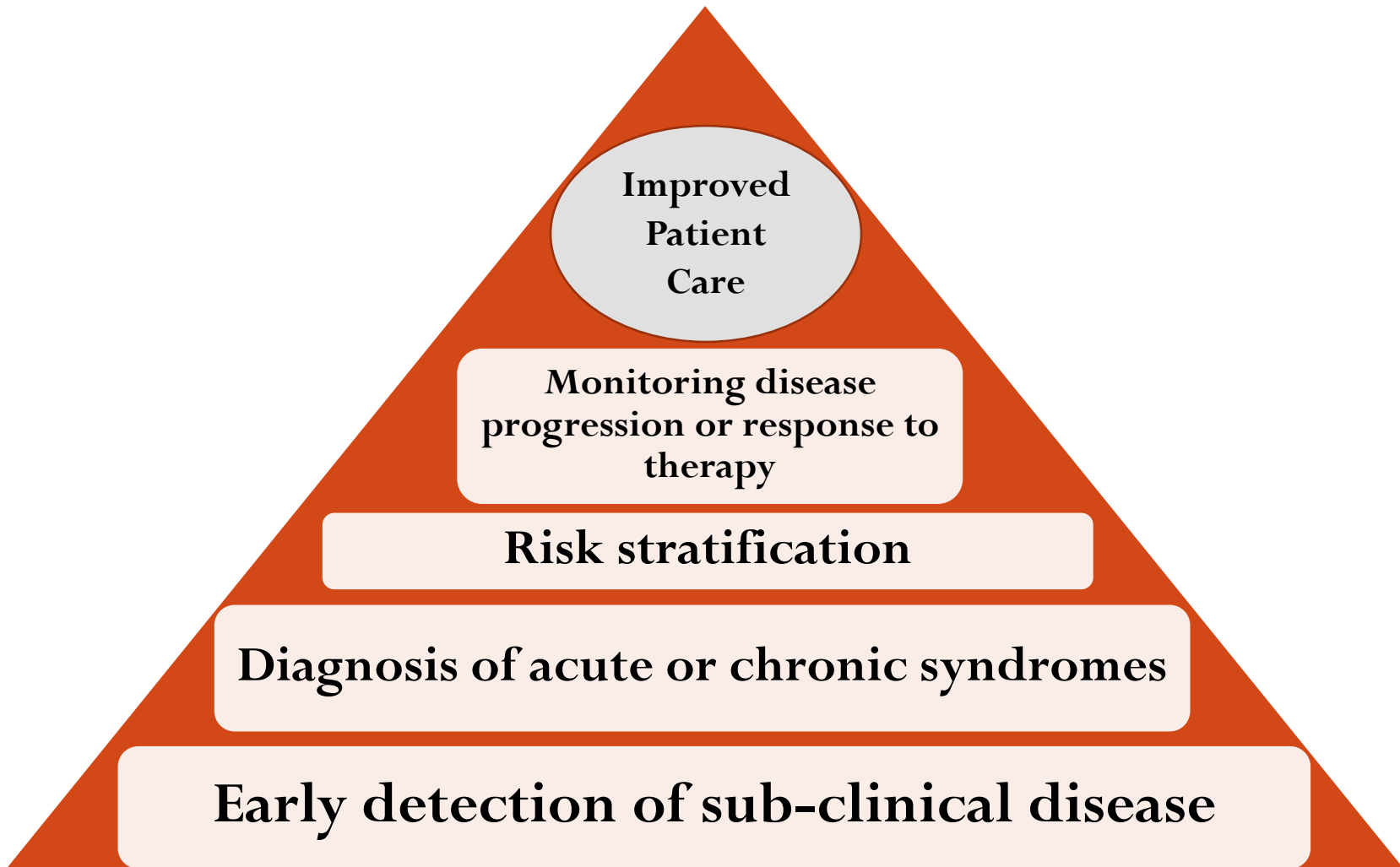
Laboratory leverages 60-70% of all
critical & Rx decisions (admission,
discharge and drug therapy)

Laboratory represents
only a small fraction of
total hospital costs <5%



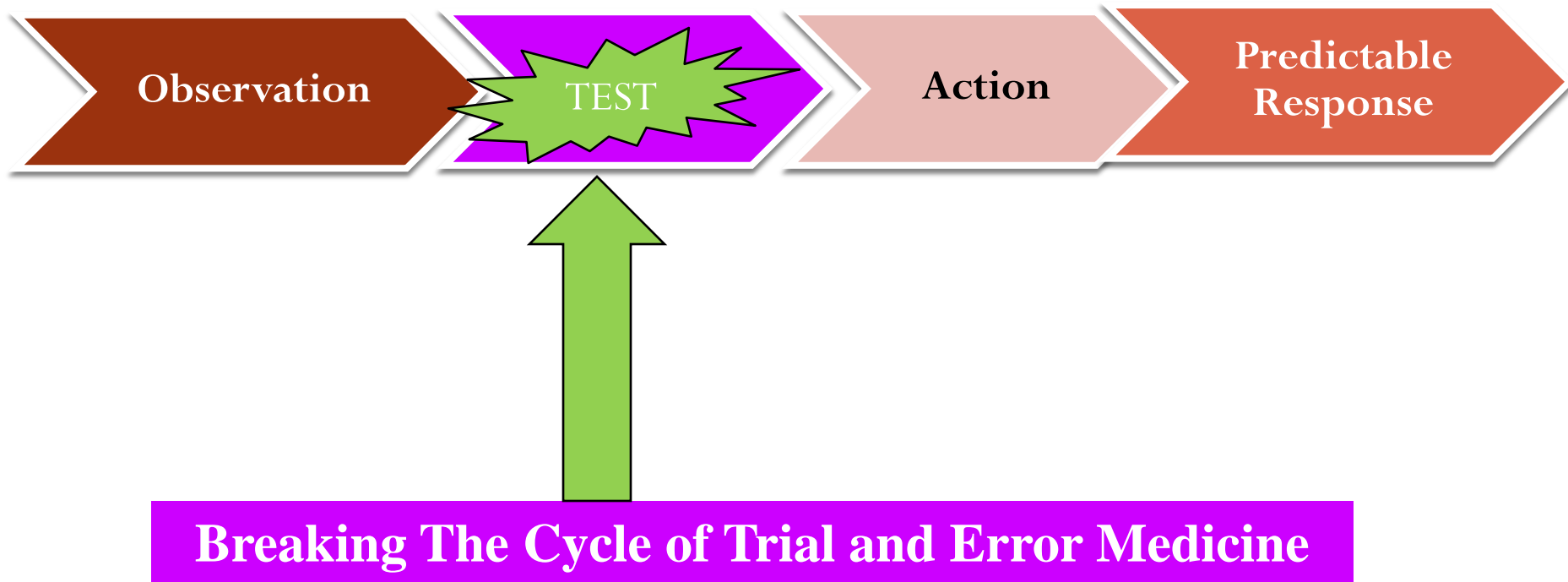
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Laboratory Medicine: a cornerstone for improved patient care!



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Linking Tests to Action and Therapy



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Patients Don't Have Time for Trial & Error

Disease	1 Year Survival
Lung cancer	42%
Colorectal cancer	76%
Chronic myeloid leukemia (CML)	93%
Heart failure	74%
End stage renal disease	78%

*2007 USRDS Annual Data Report Levy, et. al., Long-term trends in the incidence and survival from heart failure, NEJM, 2002; 347(18):1397-402
CancerMpact, MattsonJack; NCI SEER data, average across all stages at Dx*



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DIAGNOSTICS - Why is it Important?

Diagnosis Saves Lives
Diagnosis Saves Money

Monitoring Ensures Both



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Diagnostics – A Path To More Efficient And Effective Healthcare

- Cutting down health costs
- Example - Disease management tool in
CVD



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Contribution of Selected Diagnostic Tests to Avoidable Adverse Events, Deaths and Costs

Disease/ Condition	Diagnostic Test	Use	Annual Avoidable Events	Annual Avoidable Deaths	Avoidable Costs
Diabetes	HbA1c level	Manage glucose levels	14,000 heart attacks, strokes, or amputations	4,300-9,600	\$573 million
Colorectal cancer	Fecal occult blood test	Rule in risk for cancer	20,000 cases of colorectal cancer diagnosed/treated at a later stage	4,200-6,300	\$191 million
Heart disease	Cholesterol test	Assess risk for heart disease or heart attack	14,600 major coronary events	6,900-17,000	\$ 87 million

**Adapted from: The state of health care quality: industry trends and analysis. Washington, DC: National Committee for Quality Assurance, 2004.*



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Managing diseases through diagnostics : the example of CVD

**Around 18 million people died of CVD
(30% of all death globally).**

**Overall IHD is estimated to be the cause
of death for 2 million in India in 2010.**

**Of the total cost of CVD in the EU,
around 62% is due to direct health care
costs and 21% to productivity losses.**

**52 per cent of deaths from CVD in India
occur before 70 yr of age, compared
with 23 per cent in established-market
economies**



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Managing diseases through diagnostics:

Example of CVD

- **Early detection of disease**
- **Establishment of prognosis**
- **Monitor and guide therapy**
- **Cardiac biomarkers such as NT- pro BNP – all encompassing role in management of heart failure**
 - **Useful screening tool in high risk population for detection of cardiac abnormalities**
 - **Prediction of future cardiovascular events such as heart failure**
 - **Monitoring therapy - improved patient care**



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Kaplan-Meier Survival Curves Regarding Probability of Death During 1 Year for Patient Strata, According to Quartiles of NT-pro BNP



Utilizing Lab Data Through Bioinformatics / IT

Dogma:

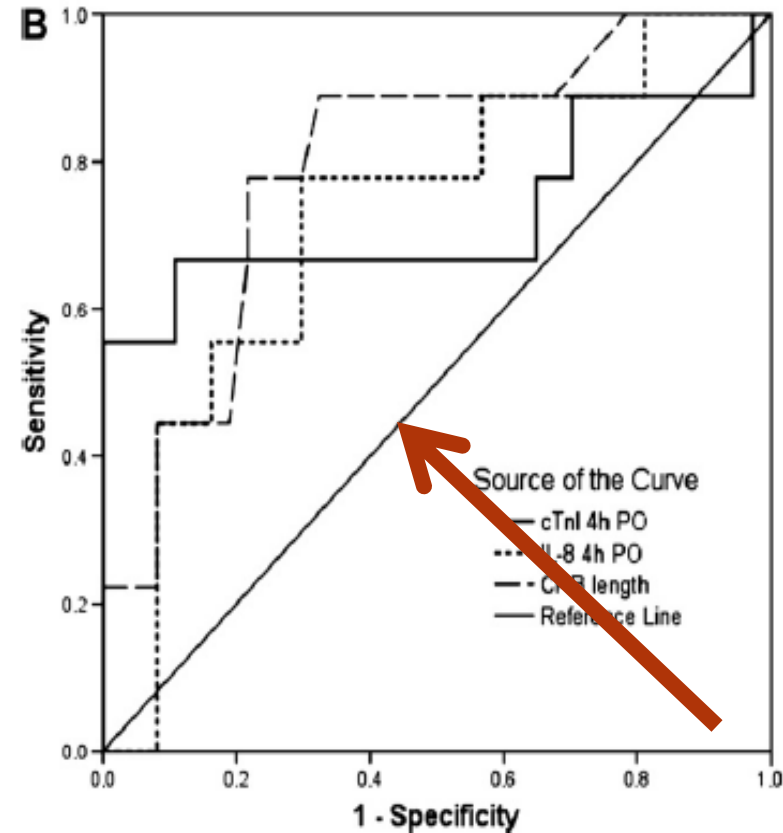
**«multifactorial diseases need multimarker
strategies»**



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Bioinformatics / IT

- Adds, combines or integrates the values of multiple biomarkers and/or variables
- 3 components: Analytical measurement, calculation, patient specific result
- Facilitates the physicians work and provides added value to diagnosis or prognosis



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Power of diagnostics to change the
focus of healthcare

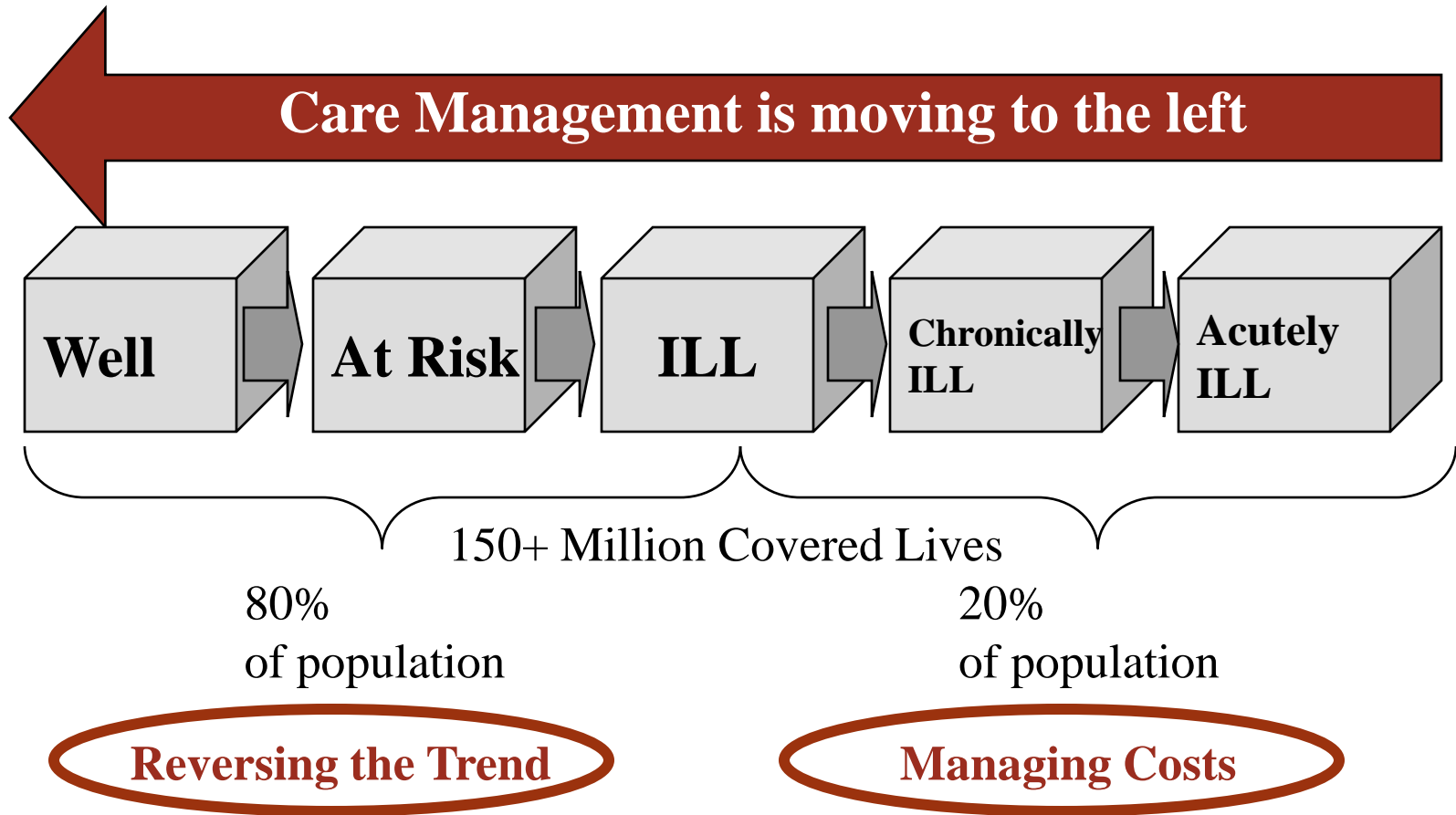
**From Treating Sickness To
Promoting Wellness**



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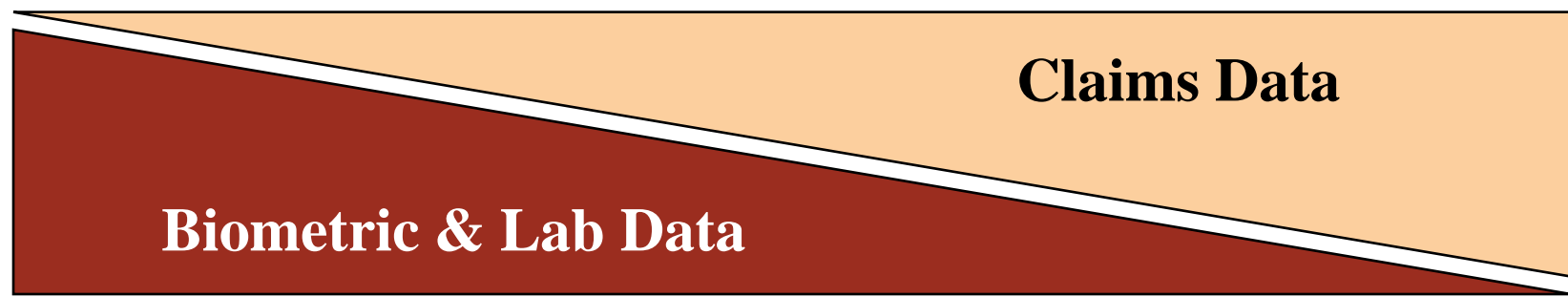
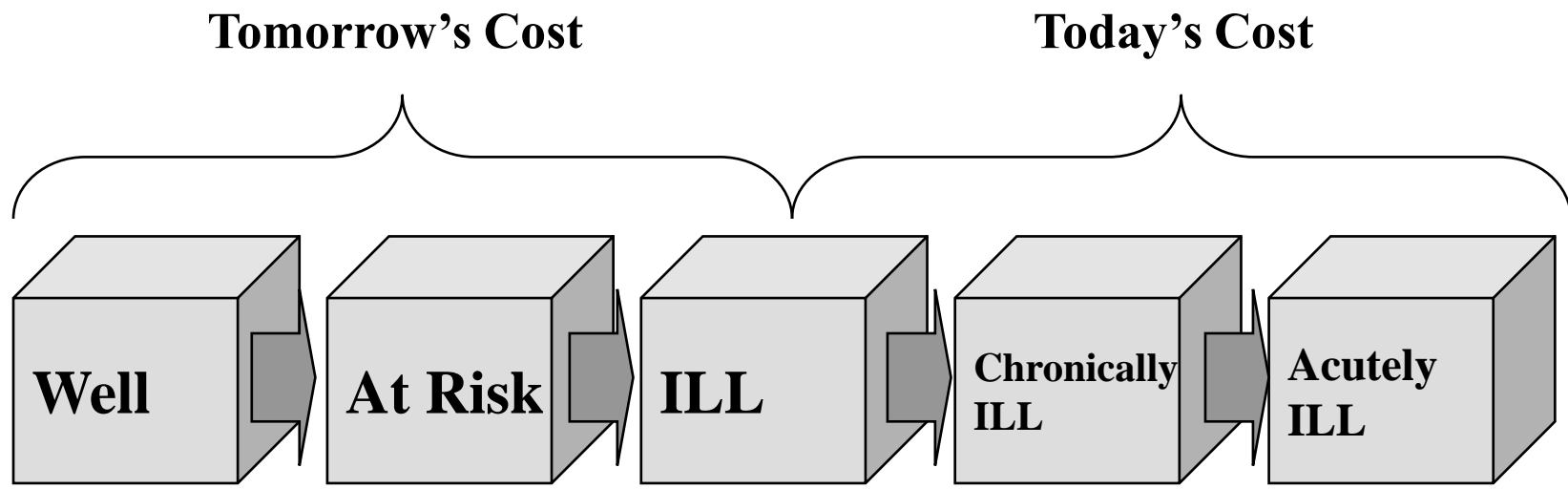
ILLNESS TO WELLNESS

- The move to total population health management



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Biometric & lab data is a key enabler



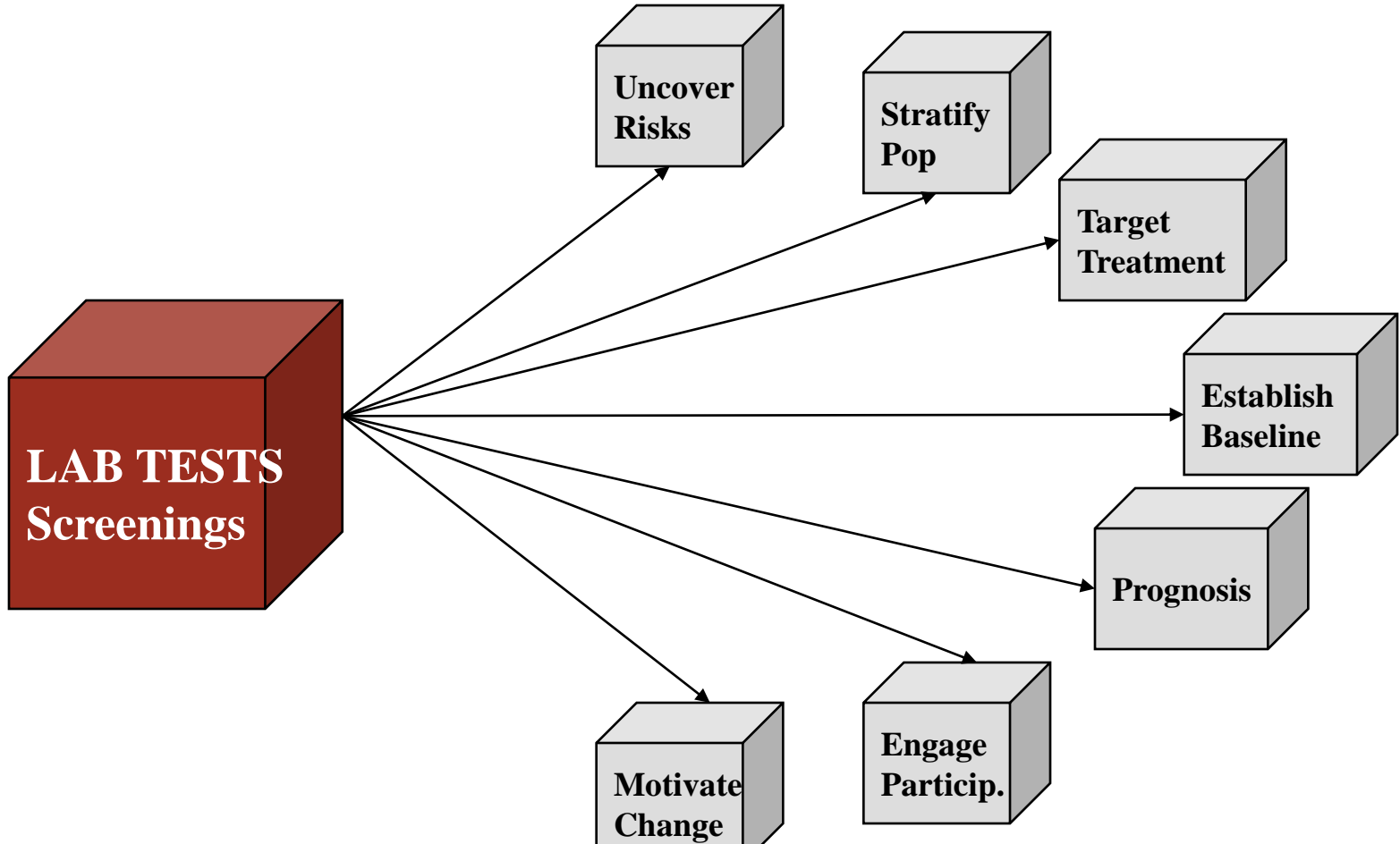
The importance of lab and statistic / biometric data

- **Claims data is too late**
 - Participant is already ill
 - Good for cost management, not cost avoidance
 - Can't help reverse the trend
- **Lab and biometric data fills in the gaps**
 - Data on those that you have no data on
 - Objective data that uncovers unknown risks
 - Provides a baseline and the data necessary to address the trend



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Debunking the myth screening

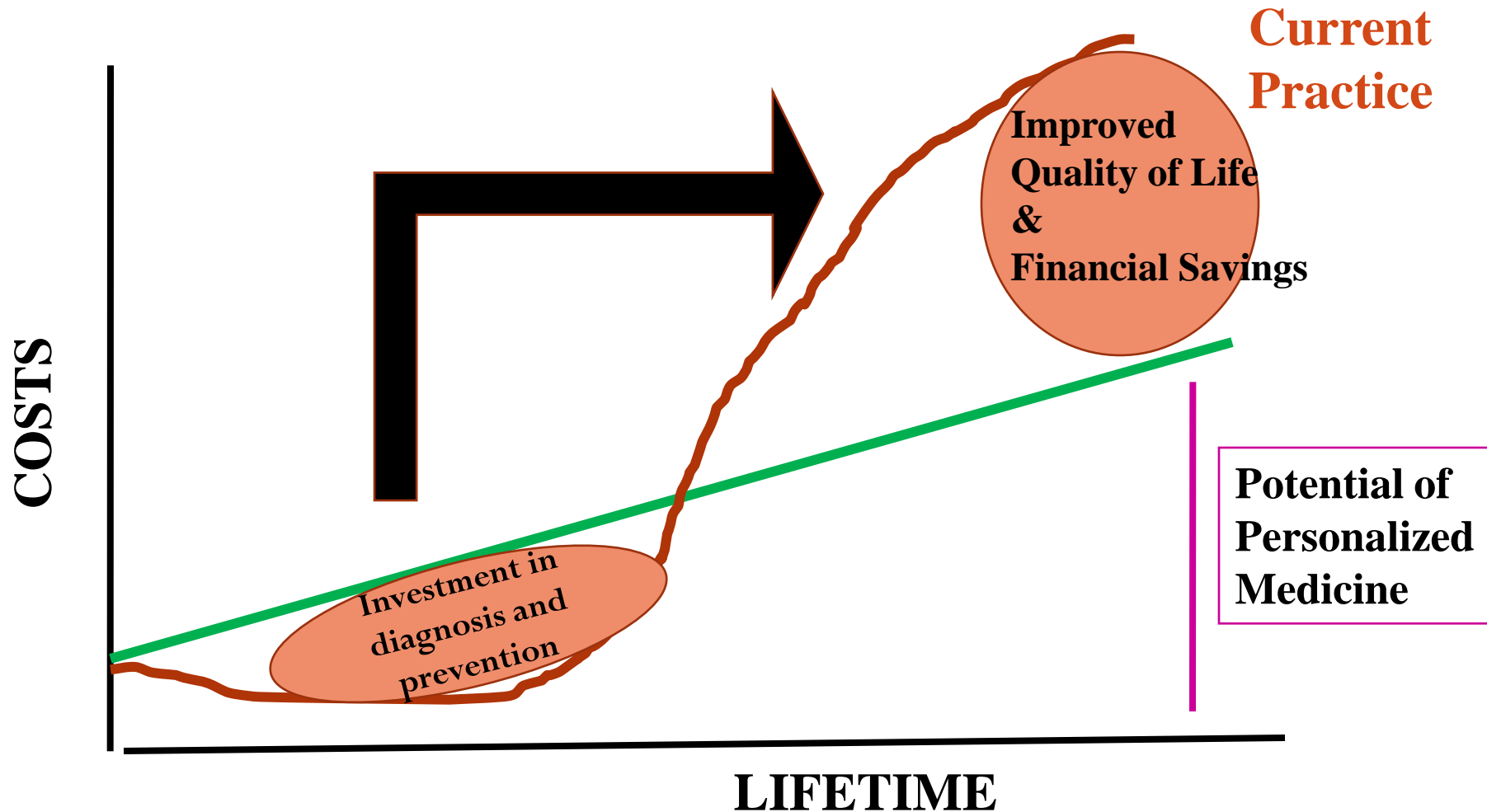


Screenings aren't an "event" but the start of a "process"



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Future Health Care Spending



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Future Directions

- **Molecular diagnostics : PCR, sequencing, microarrays; CGH**
- **Automation: enhanced robotics & informatics**
- **Point of Care testing**
- **Telemedicine**
- **Automation & molecular technology will transform diagnostic microbiology within this decade**
- **Personalized medicine**



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Personalized medicine – A reality today through molecular diagnostics



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Personalized Medicine-Pharmacogenomics

- **Mutations affect drug metabolism & efficacy**
- **Doses can be adjusted**
- **Effective drugs selected: Warfarin**
- **FDA approved assays for mutations: CYP2C9 and VKORC1 used for determining starting dose of Warfarin**



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One size fits all ?..... Approach to therapy

Pharmacogenetic (PGx) diagnostics are gene-based diagnostic tests used to determine individual benefits or harms of taking certain medications

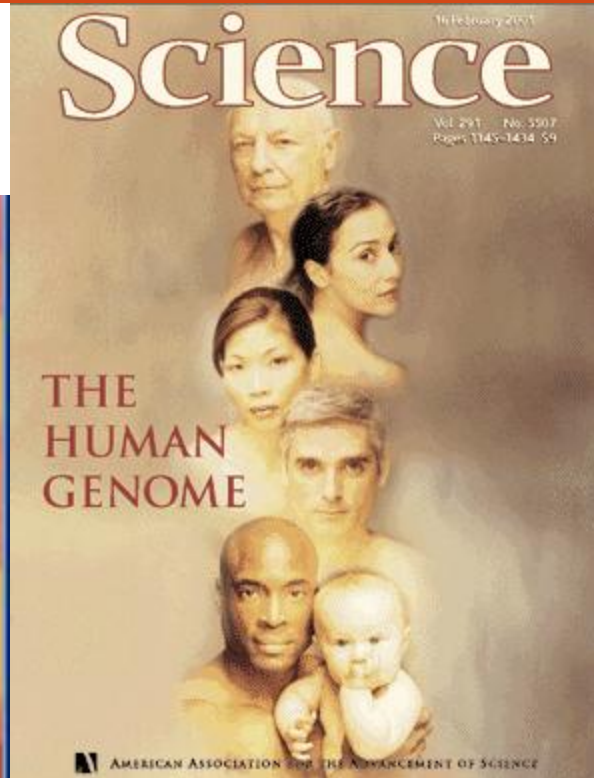
One such use of PGx links individual genetic variation to information on drug metabolism (drug breakdown and processing in the body)

Shift within the medical community from a “one size fits all” drug treatment approach to that of “right amount of the right drug for the right patient.”



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WHY NOW ?.....The Human Genome Project



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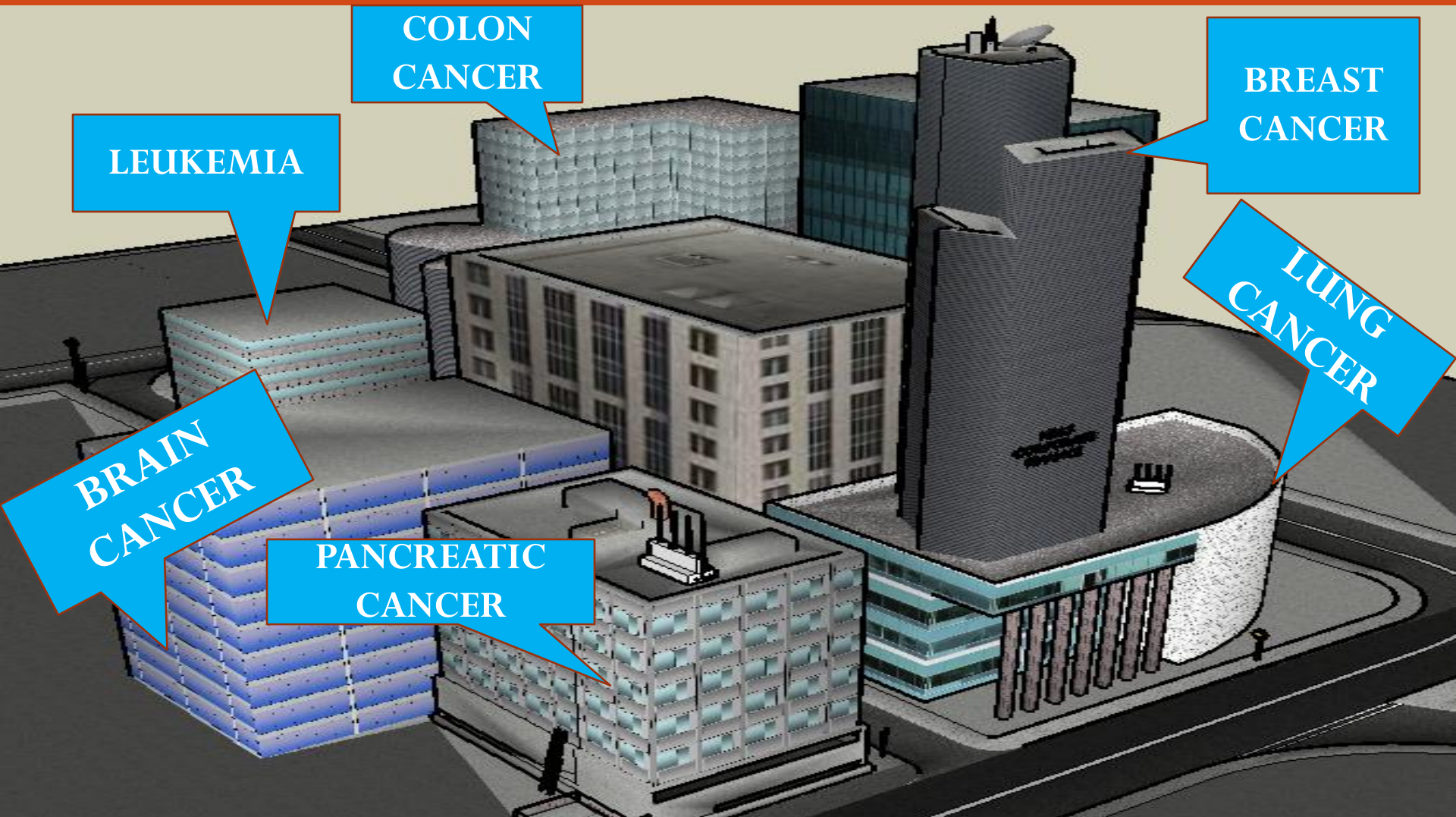
Personalized Medicine Test Categories ... some examples

CANCER	<i>Drug Selection</i>	TEST
Breast Cancer	Herceptin®	HER2
	<i>Drug Dosage</i>	
Colorectal Cancer	Camptosar®	UGT1A1
	<i>Drug Efficacy</i>	
Chronic Myelogenous Leukemia	Gleevec®	Quant BCR-ABL
	<i>Disease Status</i>	
Chronic Lymphocytic Leukemia	Campath®	Minimal Residual Disease
	<i>Recurrence Risk</i>	
Breast Cancer	Oncotype DX®	Multivariate Analysis
	<i>Predisposition</i>	
Breast Cancer	BRACAnalysis®	Gene sequencing, risk analysis



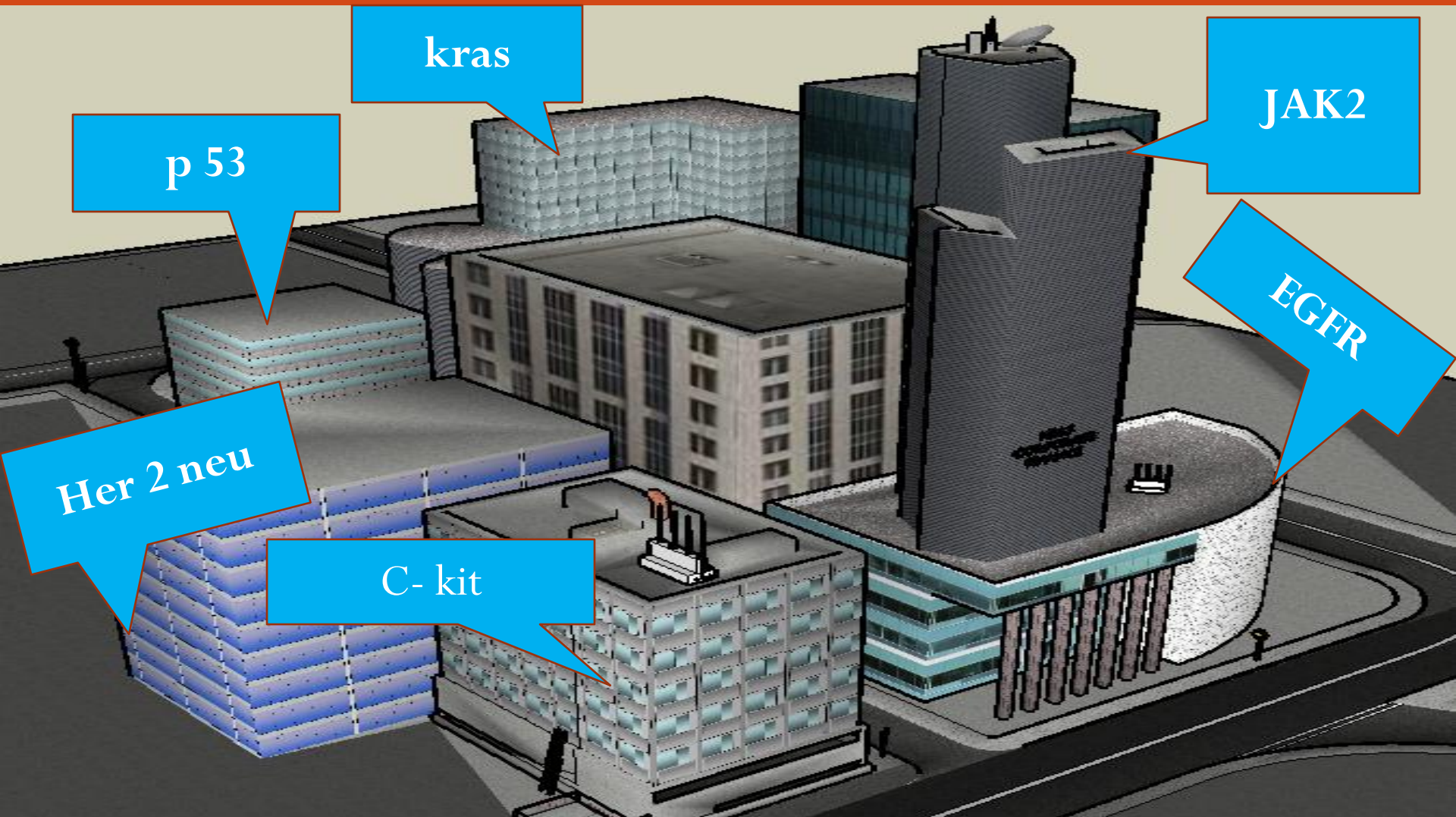
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Hospitals - TODAY



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Hospitals - TOMORROW



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Interplay of Lab disciplines is required for making a final diagnosis

Example:
Diagnosis of hematological malignancies



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Diagnosis of Hematological Malignancies

- **Clinical Features**
- **Morphology**
- **Flowcytometry**
- **Cytogenetics**
- **Molecular genetics: FISH / PCR**



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Identification of t (15;17) translocation in AML patients leads to specific treatment (ATRA)
.....which changed the overall survival from 0% - 40 years ago to 80% now

Morphology Evaluation

+

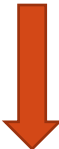
Fluorescence-Activated Cell Sorting

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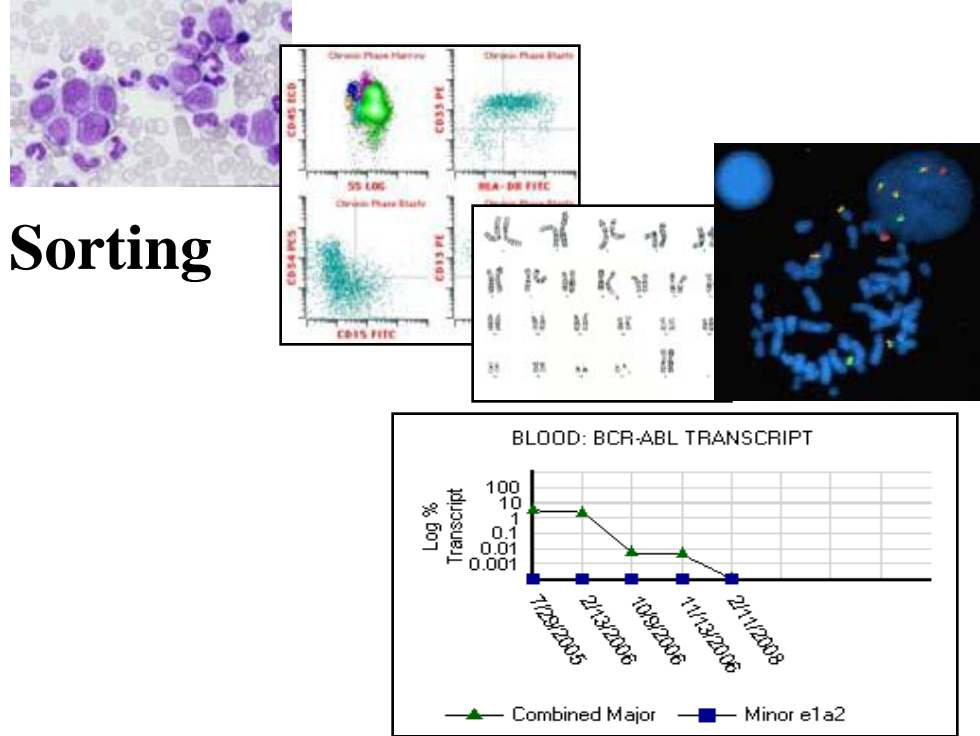
Cytogenetic Analysis

+

Molecular Analysis



Expanded Characterization and Response Prediction



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Kras testing - cost effective treatment of colon cancer

When Kras test is used to decide whether to treat with Erbitux in colon cancer patients There is...

- **60% reduction in cost per success**
- **40% of patients spared side effects from ineffective treatment**
- **Overall success rate is unchanged at 25%**

Langreth, R. (2008), 'Imclone's Gene Test Battle', Forbes.com, 16May



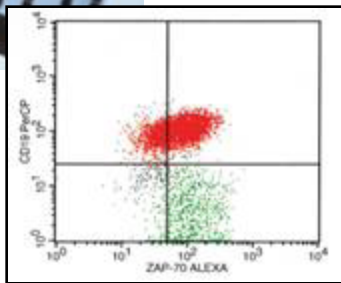
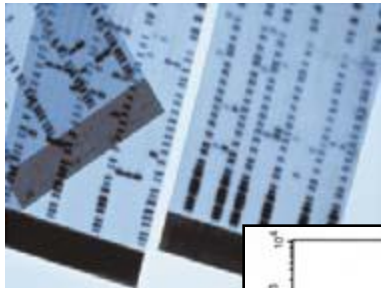
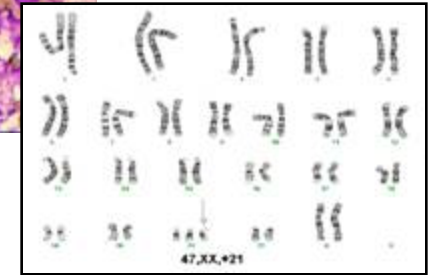
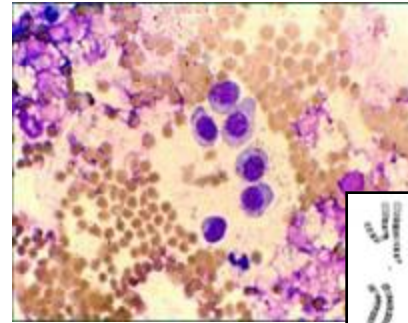
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Diagnostic Technology Has Improved

Past – Macro Level Testing

Tests differentiated disease from non-disease

Disease defined by location and size



Today – Molecular Level Testing

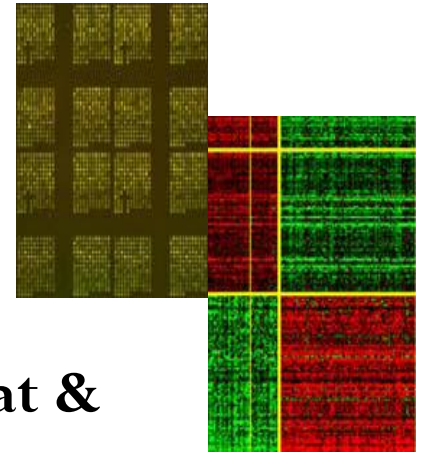
Disease defined by individual biology and /or DNA of tumor or virus

Tests to subcategorize disease:



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Tomorrow – Predictive Testing



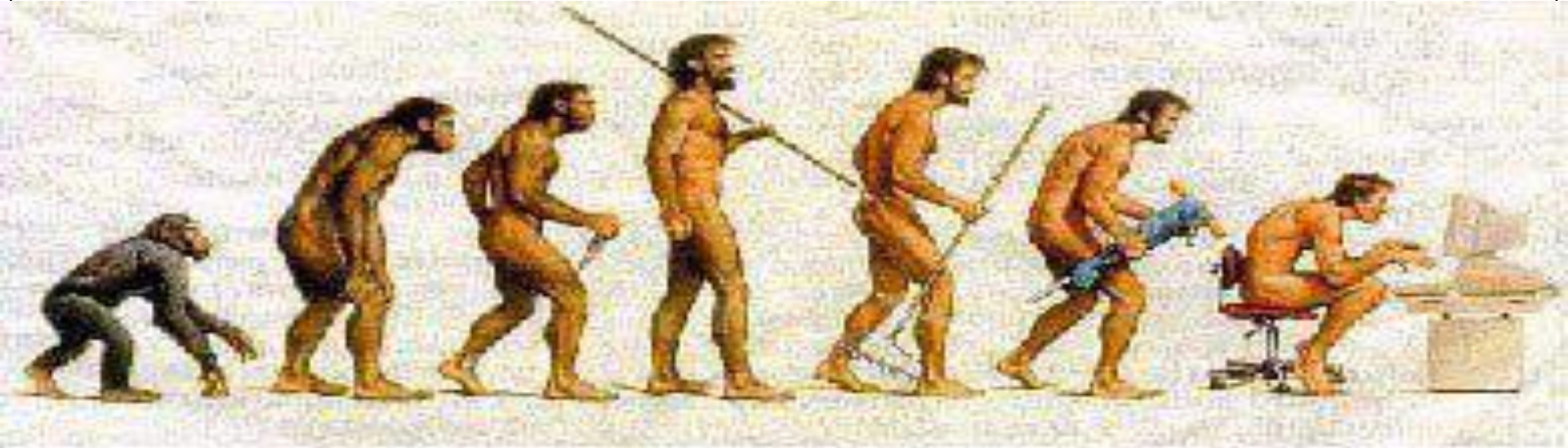
- Multiple technology platforms
- Multi-factorial testing
- Multi-gene signatures
- Multiple Sample Types – Urine, Saliva, Breath, Sweat & others?
- Increased Use of Diagnostic Imaging
- Availability of these Tests to Consumers



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How innovation can help...

...and how can we help the innovation?



Somewhere, something went terribly wrong



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EMBRACE THE "ERA OF DIAGNOSTICS"

**MAKING THE CHANGE..... FROM FEAR
TO ACCEPTANCE**



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Pathologist and Radiologists Need to :

- Own Personalized Medicine
- Source of expertise on all tests available
- Interpreter and consolidator of all test results
- Educator of all other physicians on diagnosis



Move Industry from Fear to Acceptance



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For Improved outcomes

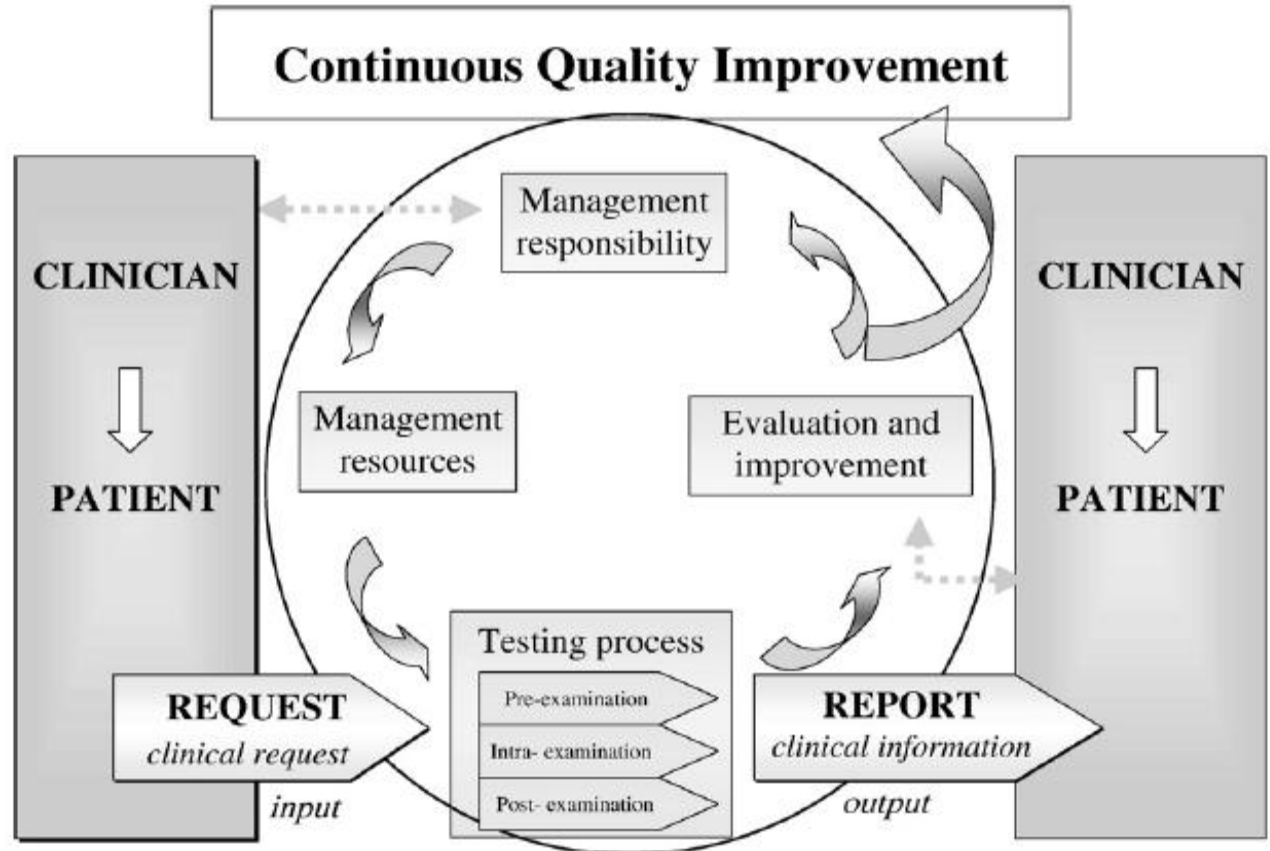
- **Publish new practice guidelines – tests and technologies**
- **Create Data on the positive outcomes and economics of appropriate use of diagnostics**
- **Regulation to encourage diagnostic & drug combinations**



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Laboratory Accreditation WHY?

- Recognition Increases the confidence in testing Laboratories
- Facilitates the acceptance of tests results



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Thank You



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