EVOLUTION OF CLINICAL TRIALS

Prof. Dr. Hamdi Akan
Ankara University Faculty of Medicine
Department of Hematology
Clinical Trials Unit
Clinical Research Association

Two Pathways of Evolution

Two Pathways of Evolution

Evolution of Human Subjects Research and Guidelines

Table. Evolution of Human Subjects Research and Guidelines

Year	Event
1932-1972	Tuskegee Syphilis Study
1939-1944	Experiments on concentration camp prisoners by Nazi scientists
1944-1974	Secret human radiation experiments
1946-1948	Guatemalan STD inoculation studies
1947	Nuremburg Code
1950	NIH Clinical Center requires informed consent for its studies
1953-1954	Sing Sing Prison syphilis inoculation study
1956-1972	Hepatitis studies at Willowbrook State School for the Retarded
1960	NIH Clinical Center requires independent ethical review for its studies
1962	Kefauver-Harris drug amendments
1963	Jewish Hospital cancer study
1964	World Medical Association Declaration of Helsinki
1966	US Surgeon General policy statement on human subjects research (IRB origin)
1971	NIH Office for Protection from Research Risks established
1974-1978	National Commission for the Protection of Human Subjects
1974	HHS regulations for human subjects research
1975	CDC Office of Human Research Protections established
1978-1983	President's Commission for the Study of Ethical Problems
1979	Belmont Report released
1981	HHS 45 CFR 46 and Food and Drug Administration 21 CFR 50, 56 regulations published
1985	NIH Clinical Center Bioethics Program founded
1991	45 CFR 46 (Common Rule) adopted
1993	CIOMS guidelines released
1994	Presidential apology for secret radiation experiments
1995	World Health Organization Guidelines for Good Clinical Practice
1996- 2001	National Bioethics Advisory Commission
1996	Department of Bioethics established at NIH Clinical Center
1997	Presidential apology for Tuskegee
1998	NIH support for bioethics training and research expanded
1999	NIH support for international research and ethics training
2000	World Health Organization operational guidelines for ethics committees
2001-2009	President's Council on Bioethics
2002	Secretary's Advisory Committee on Human Research Protections
2005	UNESCO Universal Declaration on Bioethics and Human Rights
2009	Executive order to create Presidential Commission for the Study of Bioethical Issues

Abbreviations: CDC, Centers for Disease Control and Prevention; CFR, Code of Federal Regulations; CIOMS, Council for International Organizations of Medical Sciences; HHS, Department of Health & Human Services; IRB, institutional review board; NIH, National Institutes of Health; STD, sexually transmitted disease; UNESCO, United Nations Educational, Scientific and Cultural Organization.

Frieden, T. R. et al. JAMA 2010;0:jama.2010.1554v1-2.

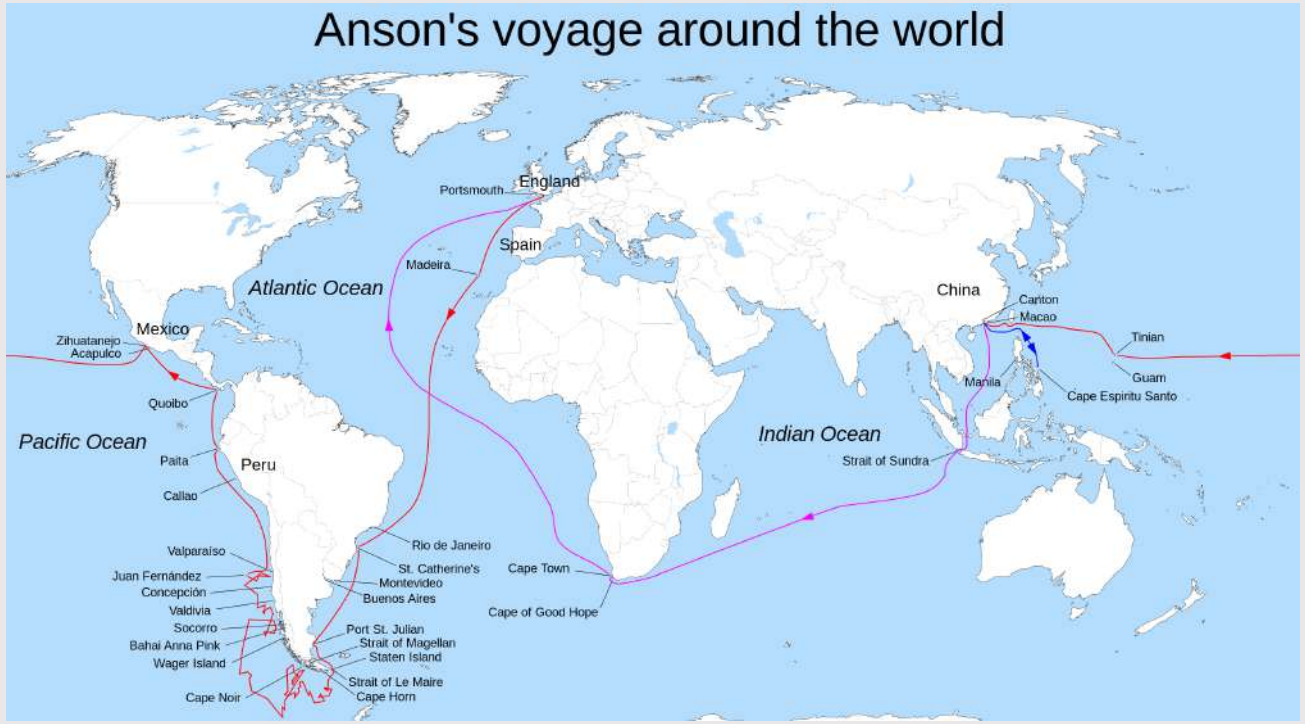
JAMA

HELSINKI


World Medical Association
Declaration of Helsinki
Ethical Principles for Medical Research
Involving Human Subjects
October 2008
INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE
ICH HARMONISED TRIPARTITE GUIDELINE
GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R1)
2% Kupfersulfat
Prot. Nr.


FØROYAR
6.50
1992
KRISTOFFUR KOLUMBUS · 1492
EUROPA

JAMES LIND (1716-1794)



1740
Commodore George Anson led a squadron of eight ships on a mission for Spain's Pacific possessions.

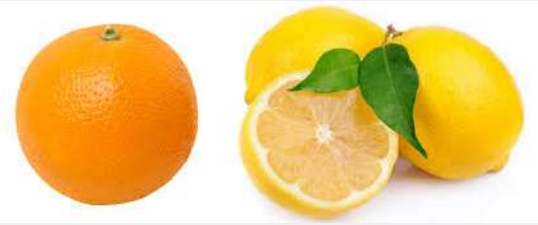
Returned to Britain in 1744

Cider

Vinegar

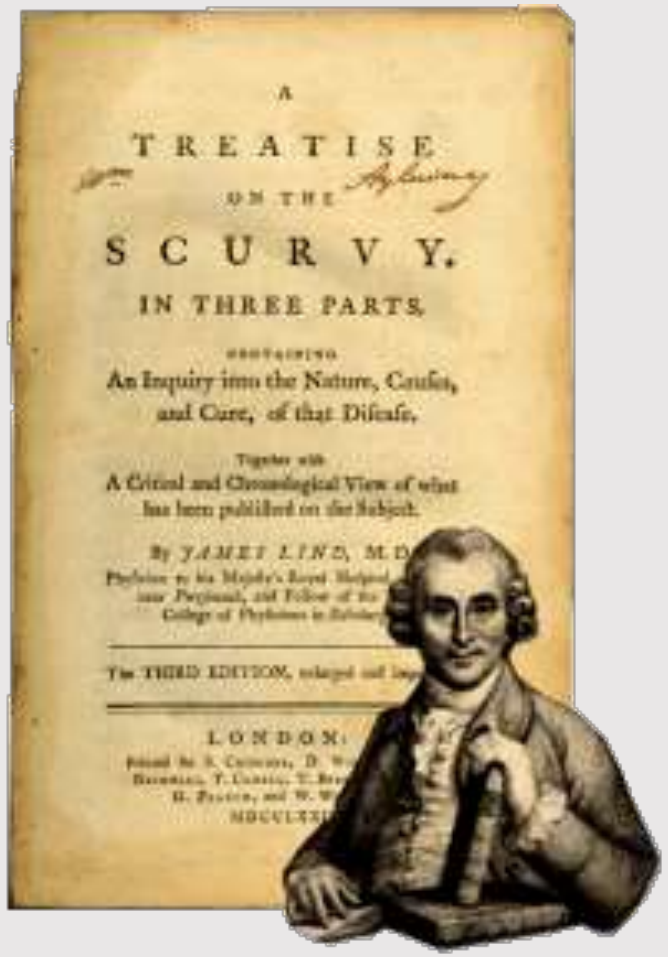
Sea water

Orange
Lemon



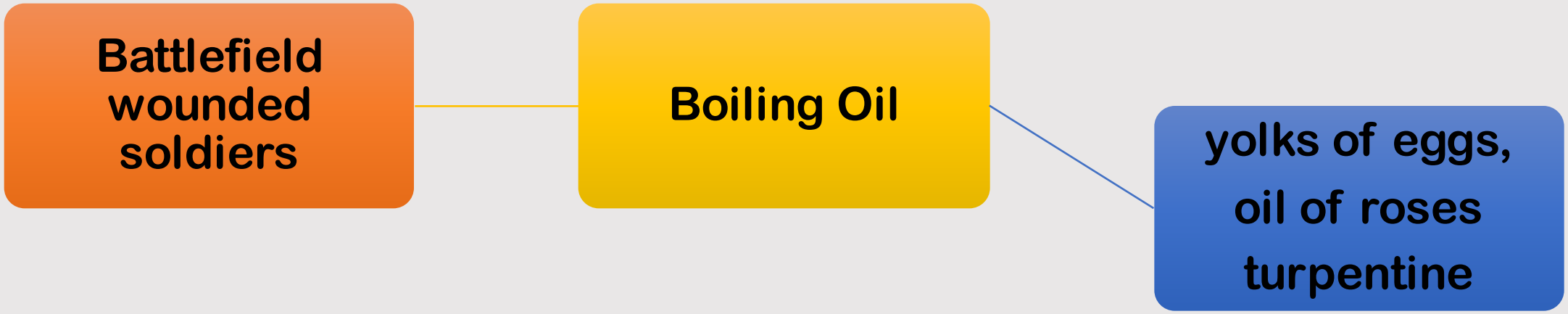
Sulfuric
acid

Herbal
Tea

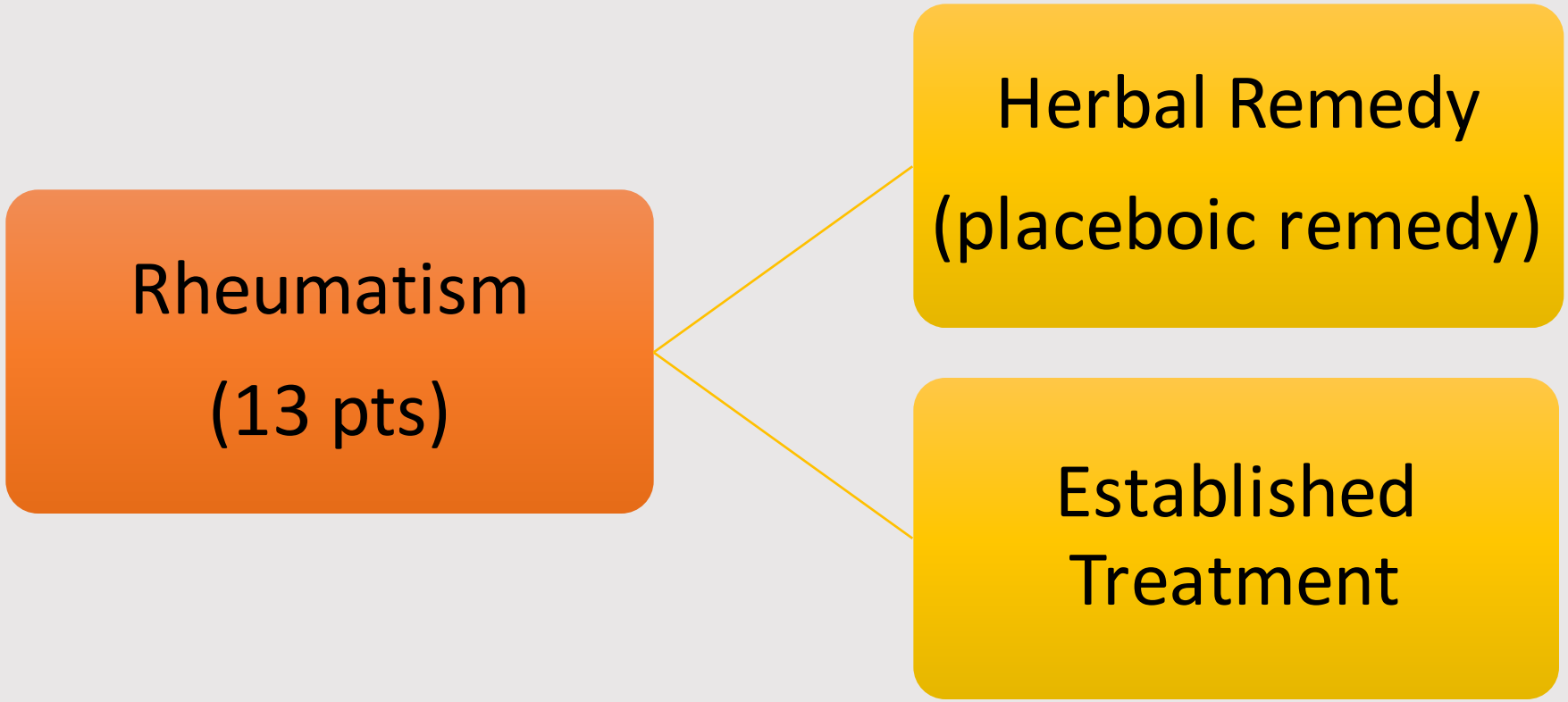

A
TREATISE
ON THE
SCURVY.
IN THREE PARTS.
An Inquiry into the Nature, Cause,
and Cure, of that Disease.
A Critical and Chronological View of what
has been published on the Subject.
By JAMES LIND, M.D.
LONDON:


Clinical Trials
Matter
International Clinical Trials' Day
20th May 2015

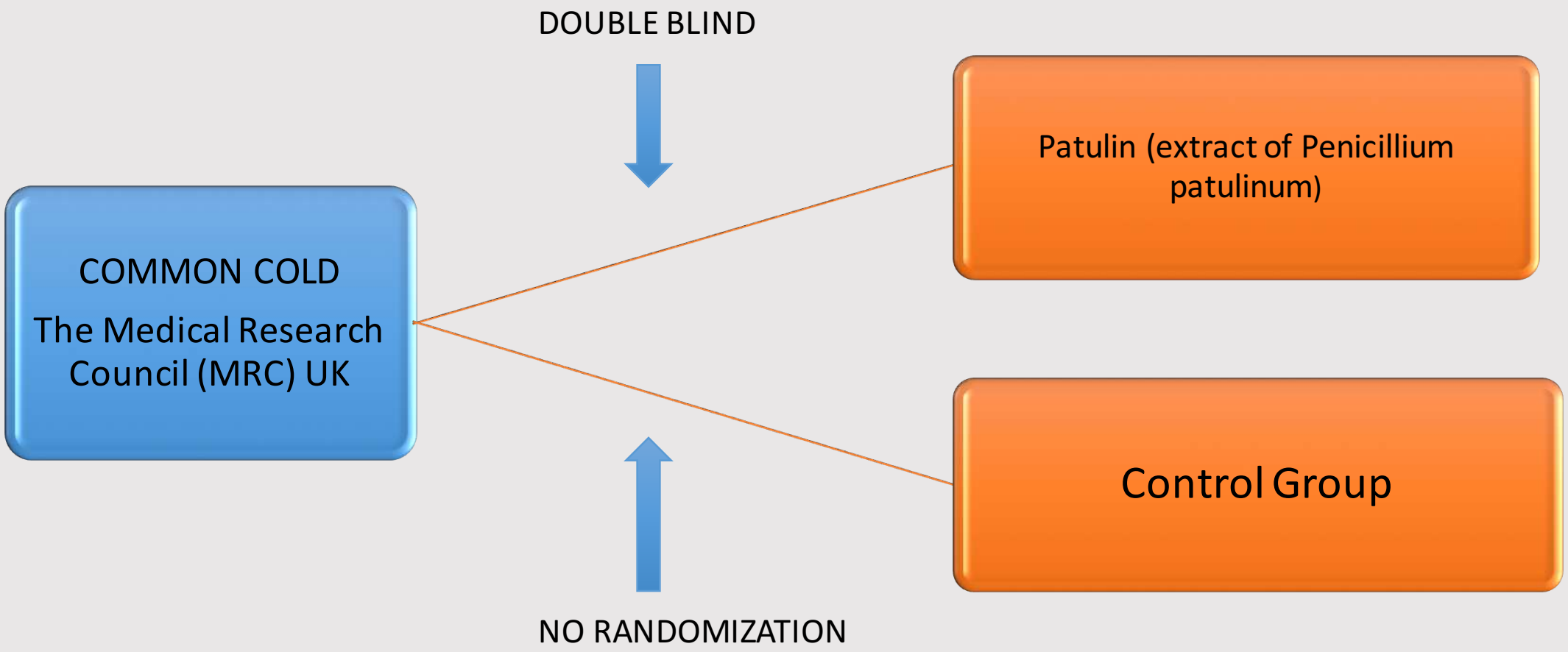
1537 - An unintended clinical trial by surgeon Ambroise Pare



1863 - First controlled clinical study by Austin Flint



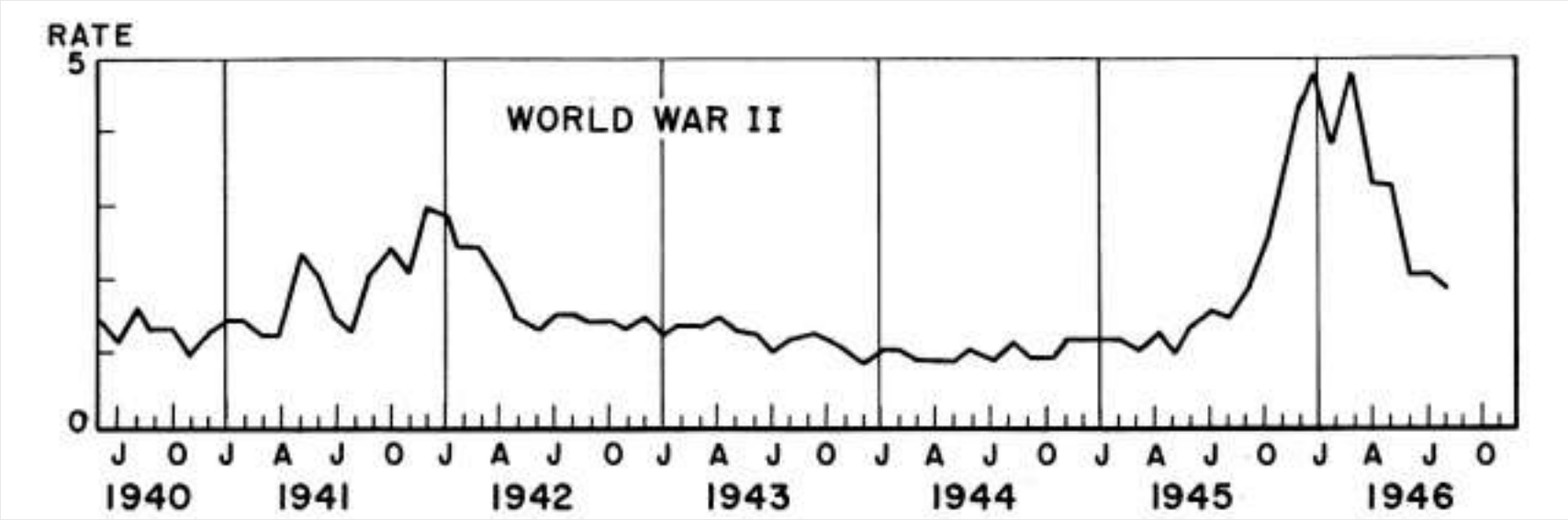
1943 - The First Double blind Controlled Trial Patulin for Common Cold



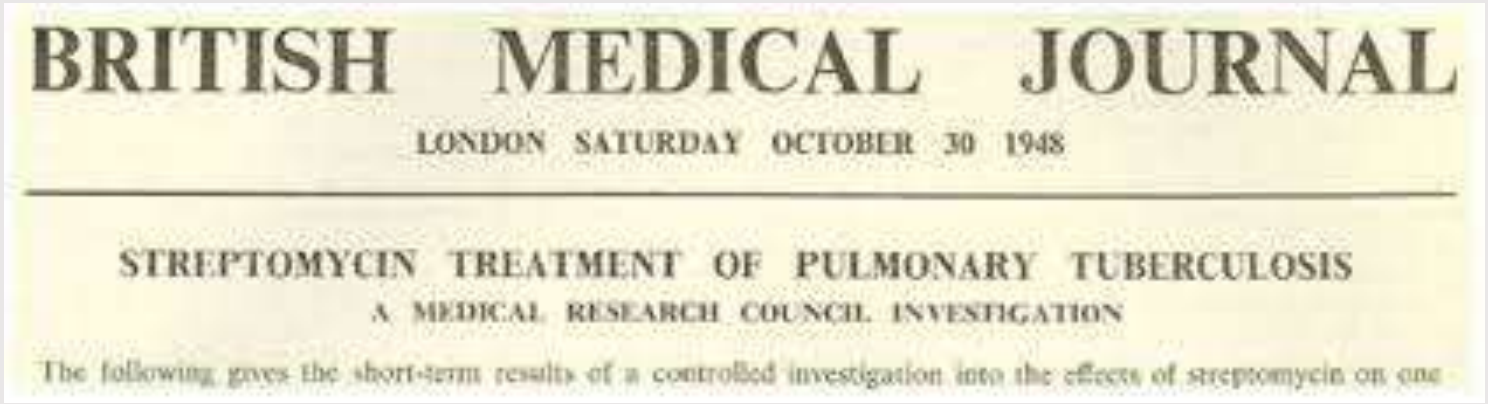
1948 - First Randomized Clinical Trial

II. WORLD WAR

Incidence of Tuberculosis



The Medical Department of the United States Army in the World War. Communicable and Other Diseases. Washington: U. S. Government Printing Office, 1928, vol. IX, pp. 171-202.



BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 30 1948

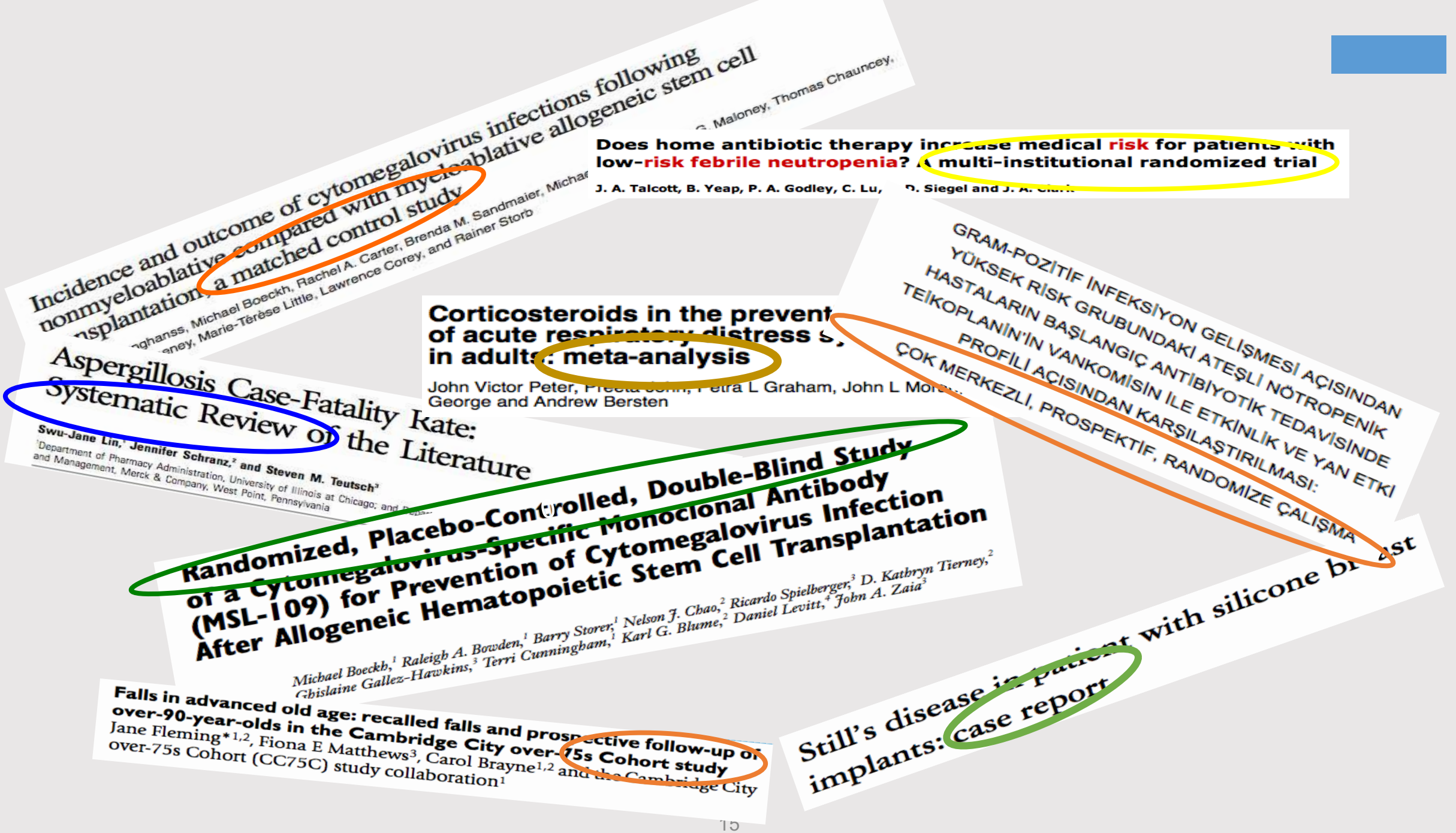
STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS

A MEDICAL RESEARCH COUNCIL INVESTIGATION

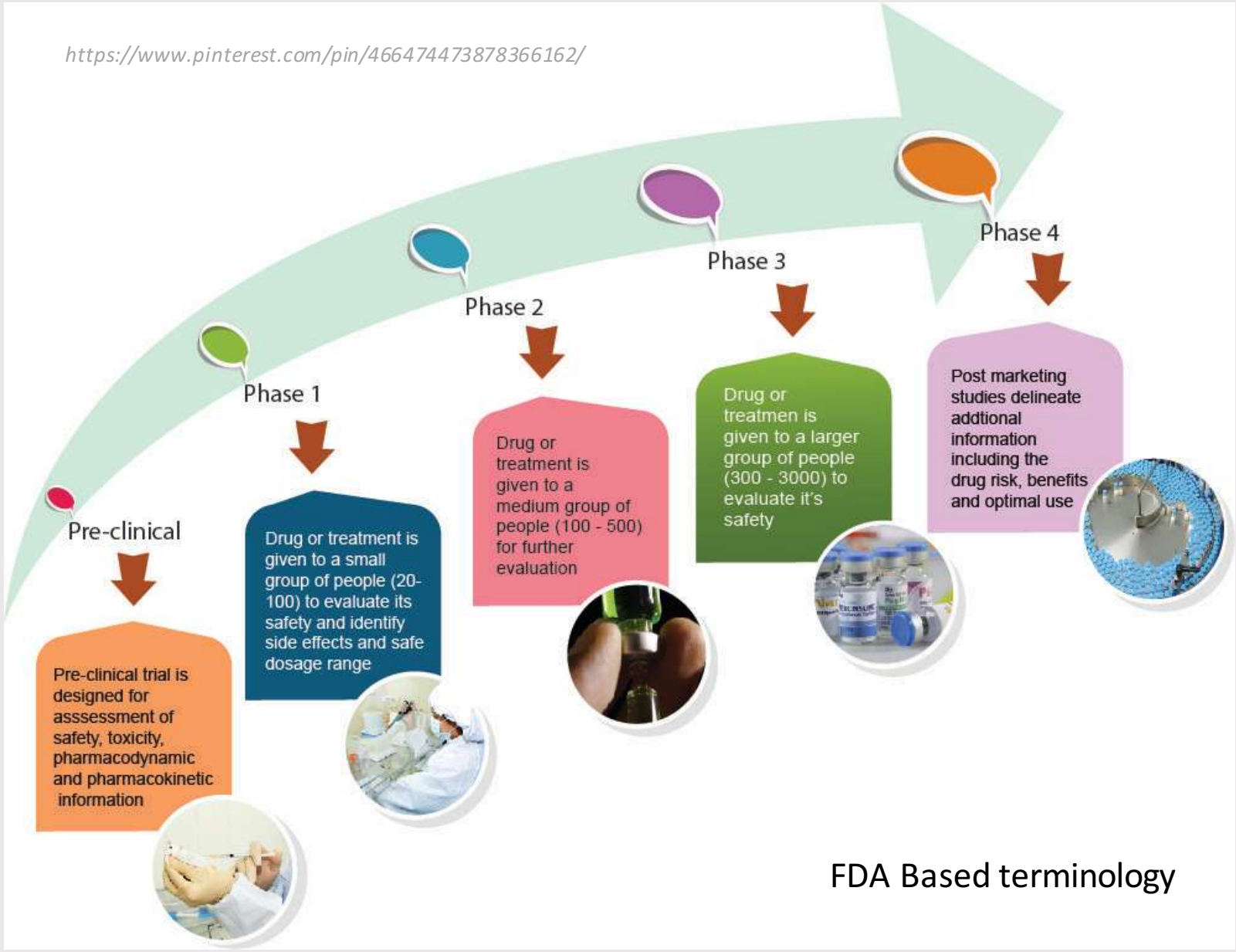
The following gives the short-term results of a controlled investigation into the effects of streptomycin on one

- The first randomized trial was published in BMJ in 1948.
- The trial was about the use of Streptomycin in soldiers with TB.
- The aim of the randomization was not scientific. Very few Streptomycin, but a lot of TB cases.

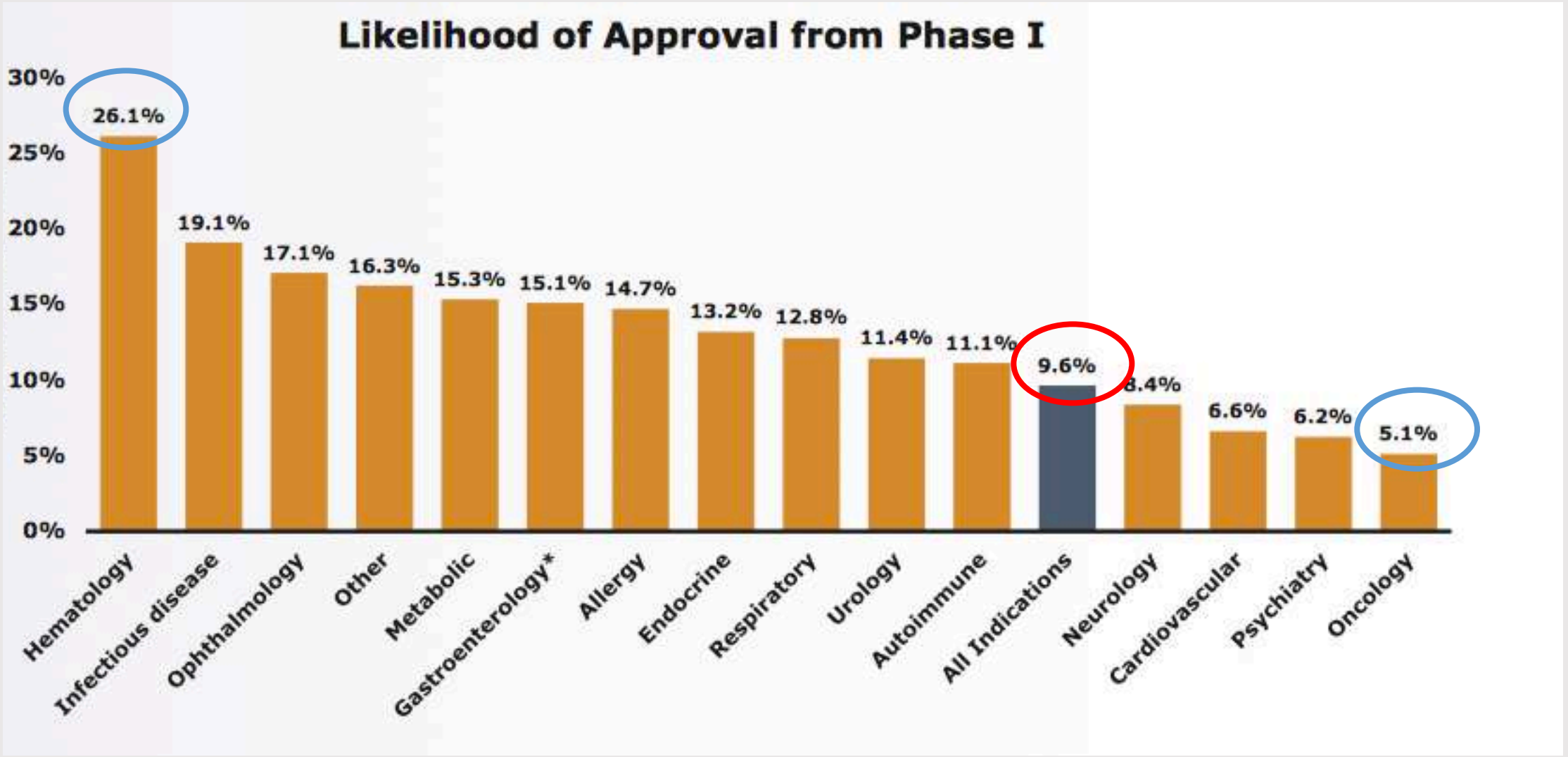
MRC Streptomycin in Tuberculosis Trials Committee. Streptomycin treatment of pulmonary tuberculosis. BMJ. 1948;2:769–83.


Incidence and outcome of cytomegalovirus infections following nonmyeloablative compared with myeloablative allogeneic stem cell transplantation, a matched control study
Does home antibiotic therapy increase medical risk for patients with low-risk febrile neutropenia? A multi-institutional randomized trial
Corticosteroids in the prevent of acute respiratory distress s in adults: meta-analysis
John Victor Peter, Petra L Graham, John L
George and Andrew Bersten
GRAM-POZİTİF İNFEKSİYON GELİŞMESİ AÇISINDAN YÜKSEK RİSK GRUBUNDAKİ ATEŞLİ NÖTROPENİK HASTALARIN BAŞLANGIÇ ANTİBİYOTİK TEDAVİSİNDE TEİKOPLANİN'İN VANKOMİSİN İLE ETKİNLİK VE YAN ETKİ PROFİLİ AÇISINDAN KARŞILAŞTIRILMASI: ÇOK MERKEZLİ, PROSPEKTİF, RANDOMİZE ÇALIŞMA
Aspergillosis Case-Fatality Kate: Systematic Review of the Literature
Swu-Jane Lin, Jennifer Schranz, and Steven M. Teutsch
Department of Pharmacy Administration, University of Illinois at Chicago; and and Management, Merck & Company, West Point, Pennsylvania
Randomized, Placebo-Controlled, Double-Blind Study of a Cytomegalovirus-Specific Monoclonal Antibody (MSL-109) for Prevention of Cytomegalovirus Infection After Allogeneic Hematopoietic Stem Cell Transplantation
Michael Boeckh, Raleigh A. Bowden, Barry Storer, Nelson J. Chao, Ricardo Spielberger, D. Kathryn Tierney, Ghislaine Gallez-Hawkins, Terri Cunningham, Karl G. Blume, Daniel Levitt, John A. Zaia
Falls in advanced old age: recalled falls and prospective follow-up of over-90-year-olds in the Cambridge City over-75s Cohort study
Jane Fleming, Fiona E Matthews, Carol Brayne and the Cambridge City over-75s Cohort (CC75C) study collaboration
Still's disease in patient with silicone breast implants: case report

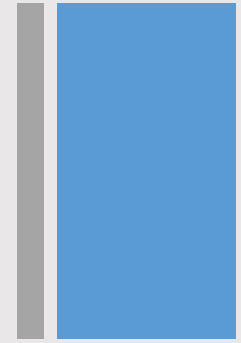
https://www.pinterest.com/pin/466474473878366162/



FDA Based terminology


Likelihood of Approval from Phase I
30%
25%
20%
15%
10%
5%
0%
26.1%
19.1%
17.1%
16.3%
15.3%
15.1%
14.7%
13.2%
12.8%
11.4%
11.1%
9.6%
8.4%
6.6%
6.2%
5.1%
Hematology
Infectious disease
Ophthalmology
Other
Metabolic
Gastroenterology*
Allergy
Endocrine
Respiratory
Urology
Autoimmune
All Indications
Neurology
Cardiovascular
Psychiatry
Oncology

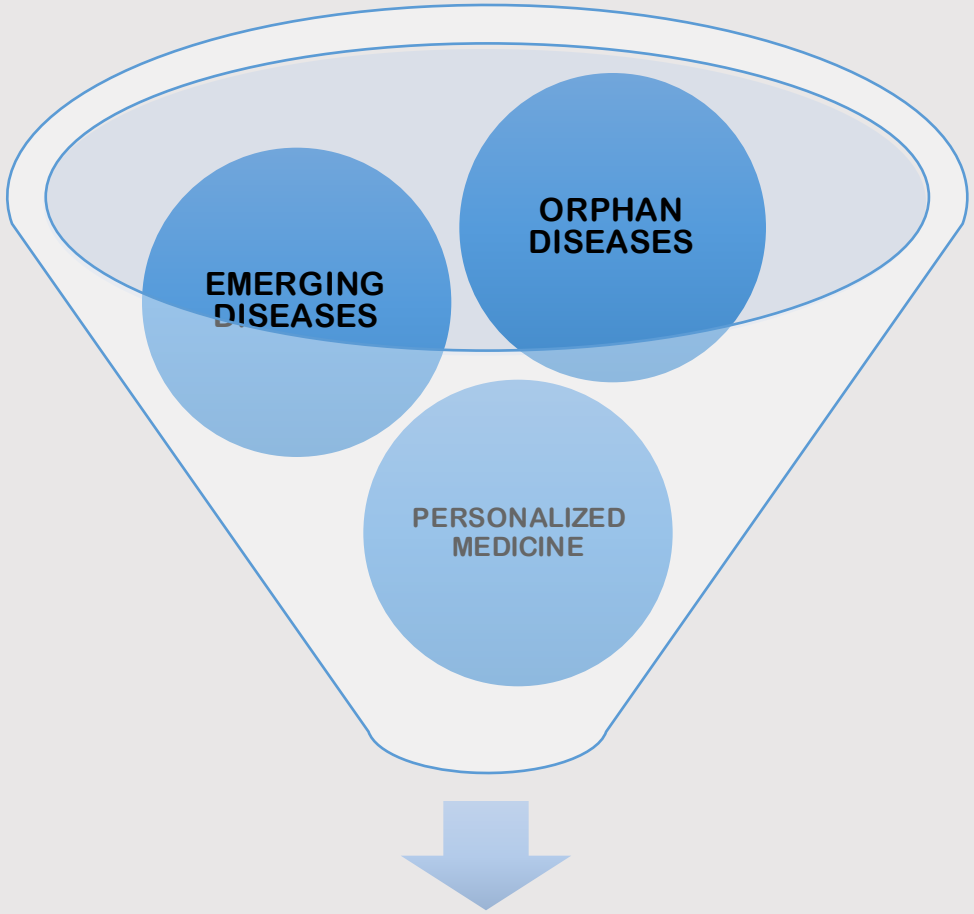
%9.6



WHY?

WHY DO WE NEED TO MODIFY THIS?

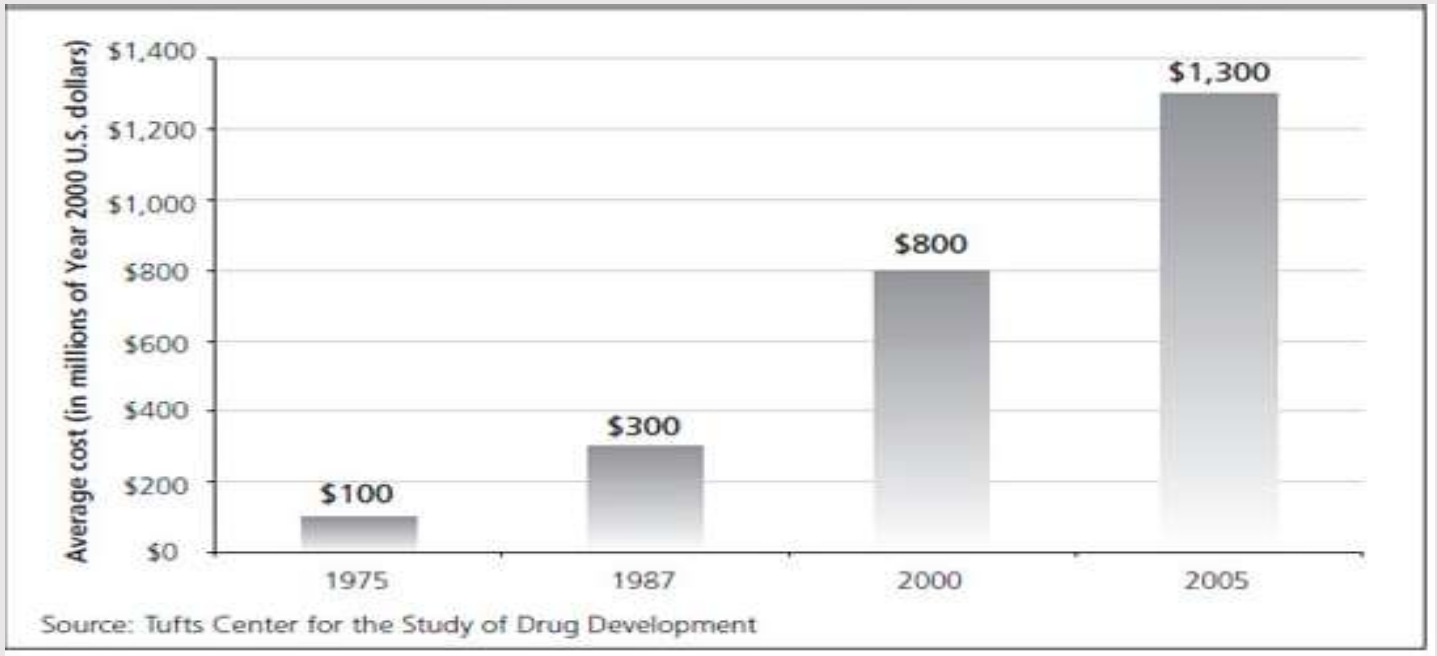
- TIME & COST
- EMERGING DISEASES
- ORPHAN DISEASES
- PERSONALIZED MEDICINE

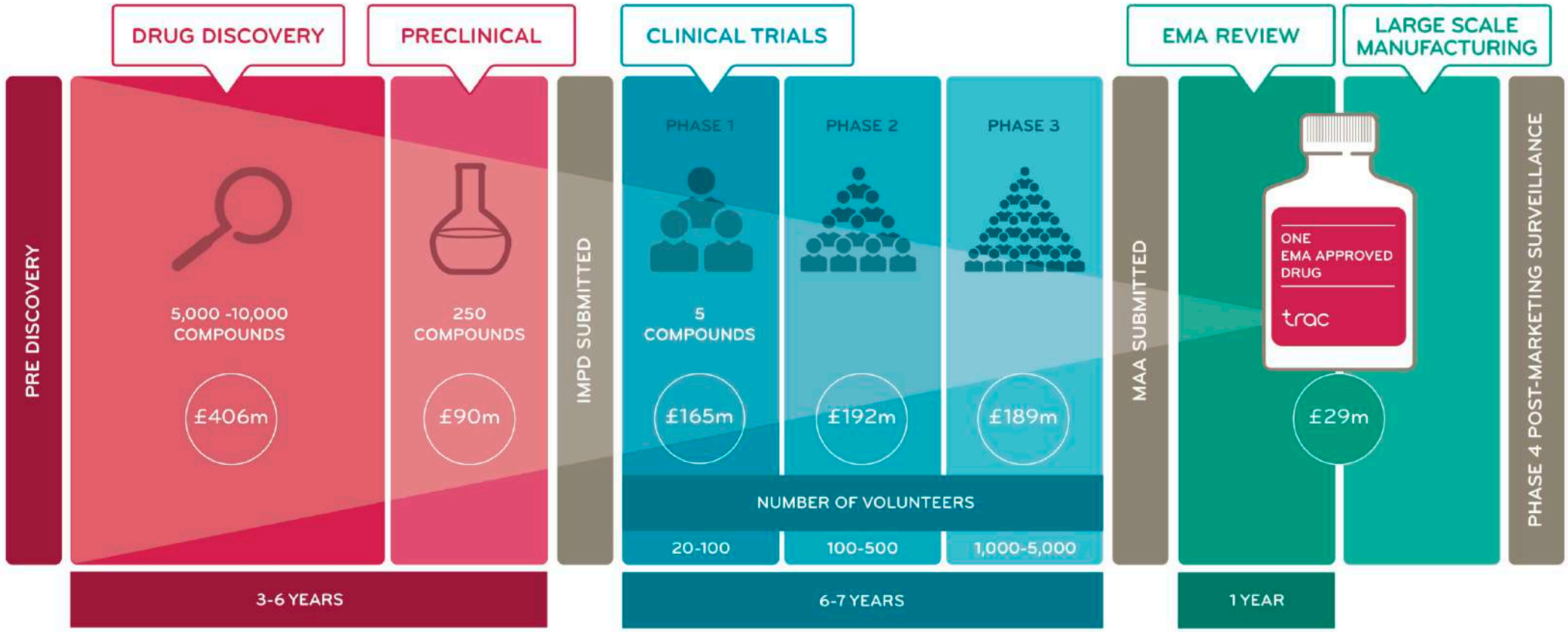


COST

The cost of a new drug approval in USA

500.000.000 – 1.000.000.000 USD.



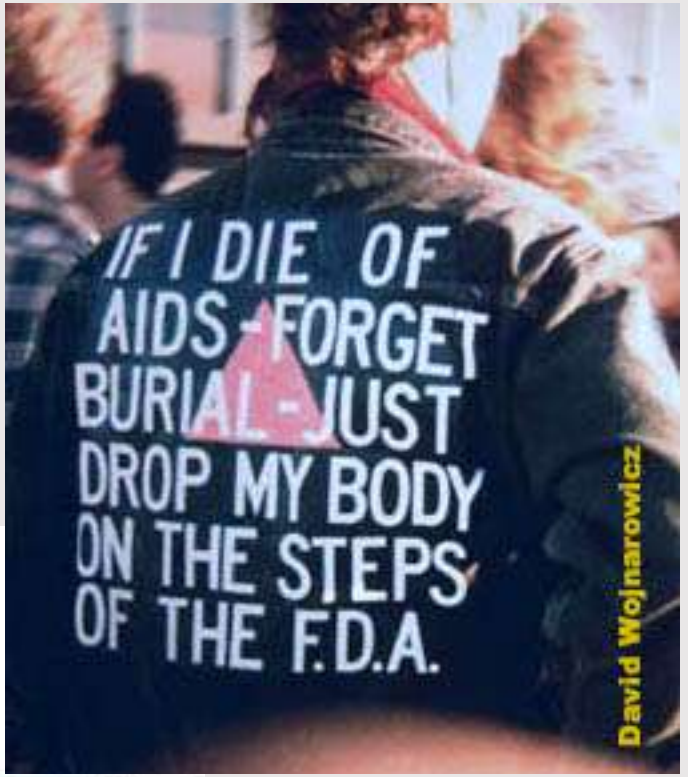

DRUG DISCOVERY
PRECLINICAL
CLINICAL TRIALS
EMA REVIEW
LARGE SCALE MANUFACTURING
PRE DISCOVERY
5,000 -10,000 COMPOUNDS
£406m
250 COMPOUNDS
£90m
IMPD SUBMITTED
PHASE 1
PHASE 2
PHASE 3
5 COMPOUNDS
£165m
£192m
£189m
NUMBER OF VOLUNTEERS
20-100
100-500
1,000-5,000
MAA SUBMITTED
ONE EMA APPROVED DRUG
trac
£29m
PHASE 4 POST-MARKETING SURVEILLANCE
3-6 YEARS
6-7 YEARS
1 YEAR

>12 YEARS

Table I. Changes in Clinical Trials: Resources, Length, and Participation

Function	1999	2005	Percent Change
Median procedures per trial protocol (e.g., blood work, routine exams, x-rays, etc.)	96	158	65%
Average clinical trial staff work burden, work-effort units	21	35	67%
Average length of clinical trial, days	460	780	70%
Clinical trial participant enrollment rate (% of volunteers meeting trial criteria)	75%	59%	-21%
Clinical trial participant retention rate (% of participants completing trial)	69%	48%	-30%

Source: Tufts Center for the Study of Drug Development, Impact Report 10, No. 1 (2008)



NIH accelerates clinical trials of Ebola vaccines

November / December 2014 | Volume 13, Issue 6

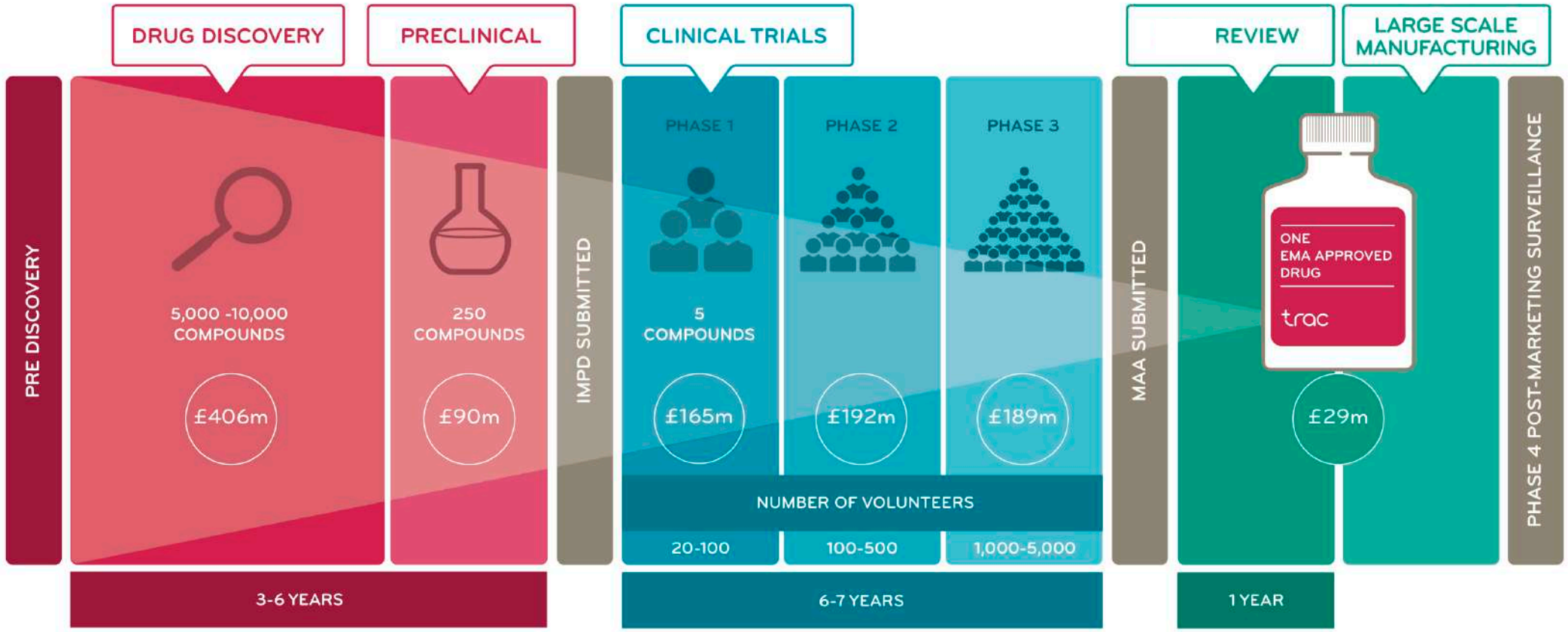
▸ Full November / December 2014 Global Health Matters newsletter [PDF <1M]

The NIH is helping guide two front-runner Ebola vaccine candidates through early-stage human trials and, barring safety or immunity problems, may have the vaccines ready for advanced testing in African and other volunteers as early as December, according to NIH officials.

Researchers at the National Institute of Allergy and Infectious Diseases (NIAID) are evaluating a vaccine developed by Canadian scientists, called VSV-ZEBOV, for safety and its ability to generate an immune system response in healthy adults who are given two intramuscular doses. The Walter Reed Army Institute of Research is simultaneously testing the vaccine candidate as a single dose at its Clinical Trials Center in Silver Spring, Maryland.

Photo by Morgana Wingar

HOW?



AUTHORITY REVIEW

METHODOLOGY

FDA EXPEDITED REVIEW

- **Accelerated Approval**
- **Priority Review**
- **Fast Track**
- **Breakthrough Therapy**

A drug candidate that addresses a serious condition and which may offer a meaningful advantage over available therapies. Uses a surrogate endpoint.
Designed for a very serious condition, the trials have been completed with an significant improvement. Review time is reduced from 10 months down to 6 months.
For drug candidates intended to treat a serious condition and that demonstrated in non-clinical studies the potential to address an unmet medical need.
A drug candidate that is intended to treat a serious condition and, also has preliminary clinical evidence to suggest it may be a substantial improvement over available therapies.

All of these programs are aimed at serious and life-threatening diseases.

HOW?

CHANGING THE METHODOLOGY

METHODOLOGY

1. USING DIFFERENT/SURROGATE END POINT/S
2. DEVELOPING NEW BIOMARKERS
3. BASKET/UMBRELLA TRIALS
4. ADAPTIVE DESIGN
5. REAL LIFE DATA (BIG DATA)

SURROGATE END POINT
VERSUS
CLINICAL END POINT

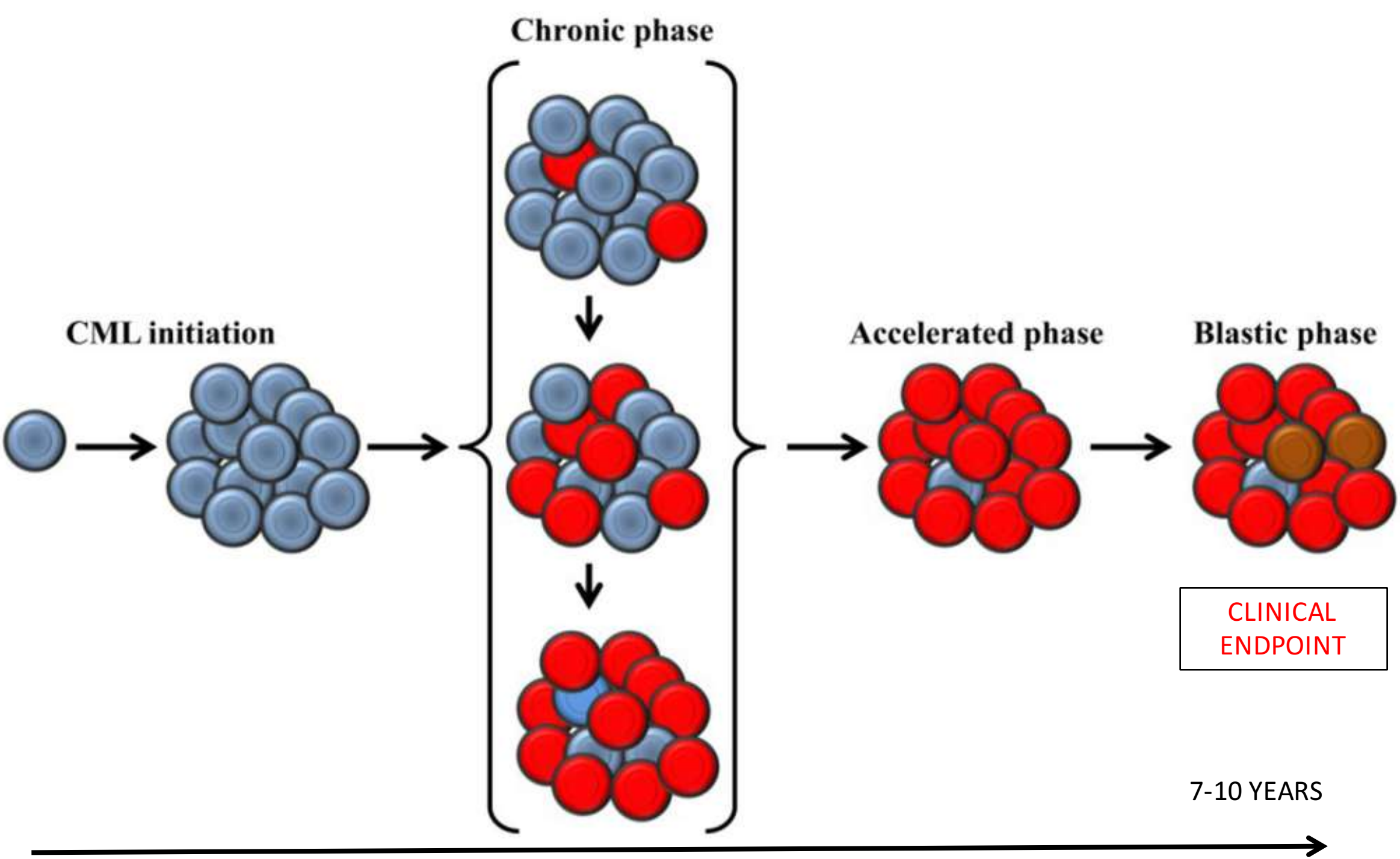
Surrogate end-point:

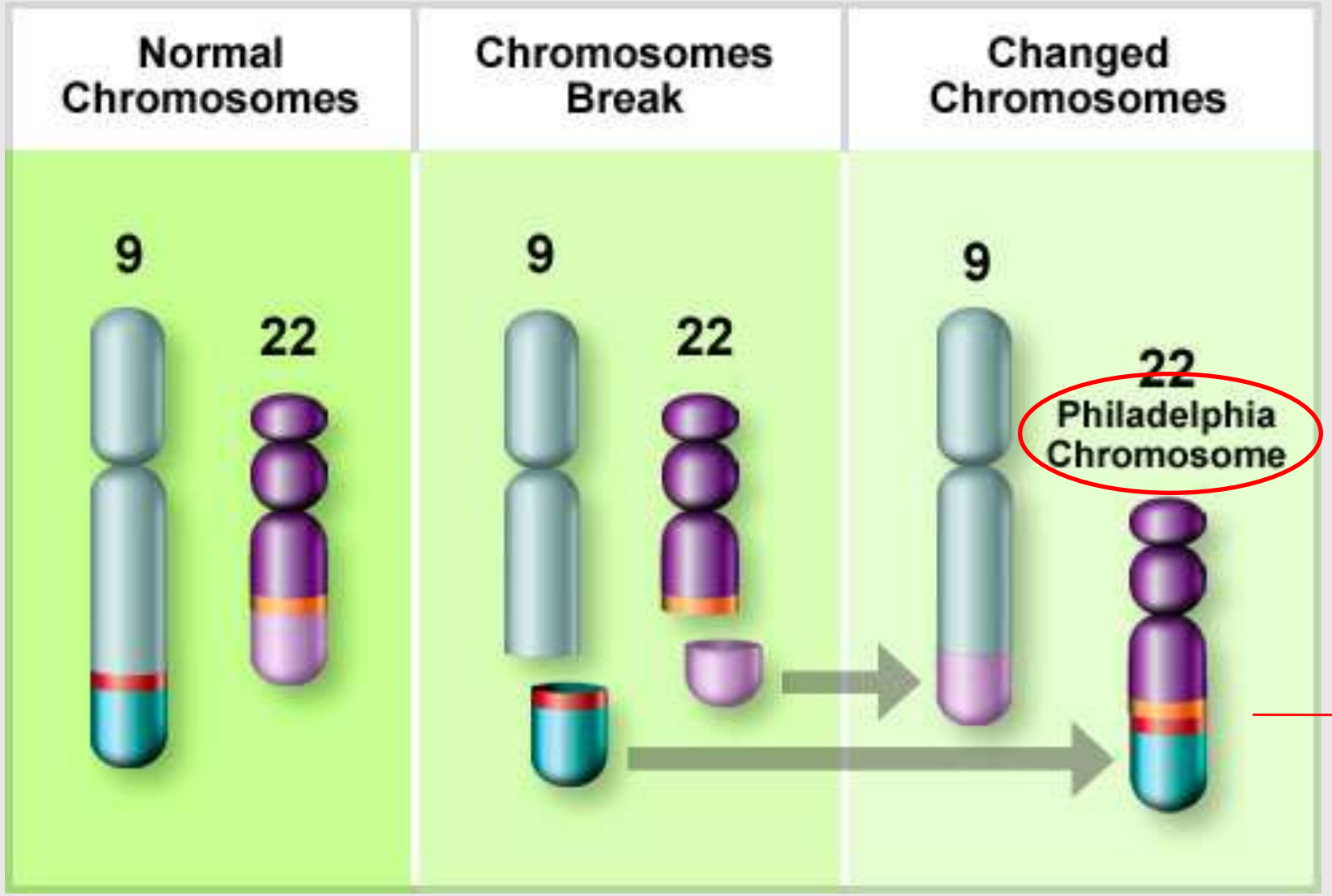
indicators of a change in the disease that are likely to predict a clinical benefit

- provide an estimate of how well a drug will treat a disease or condition

28 MAY 2001

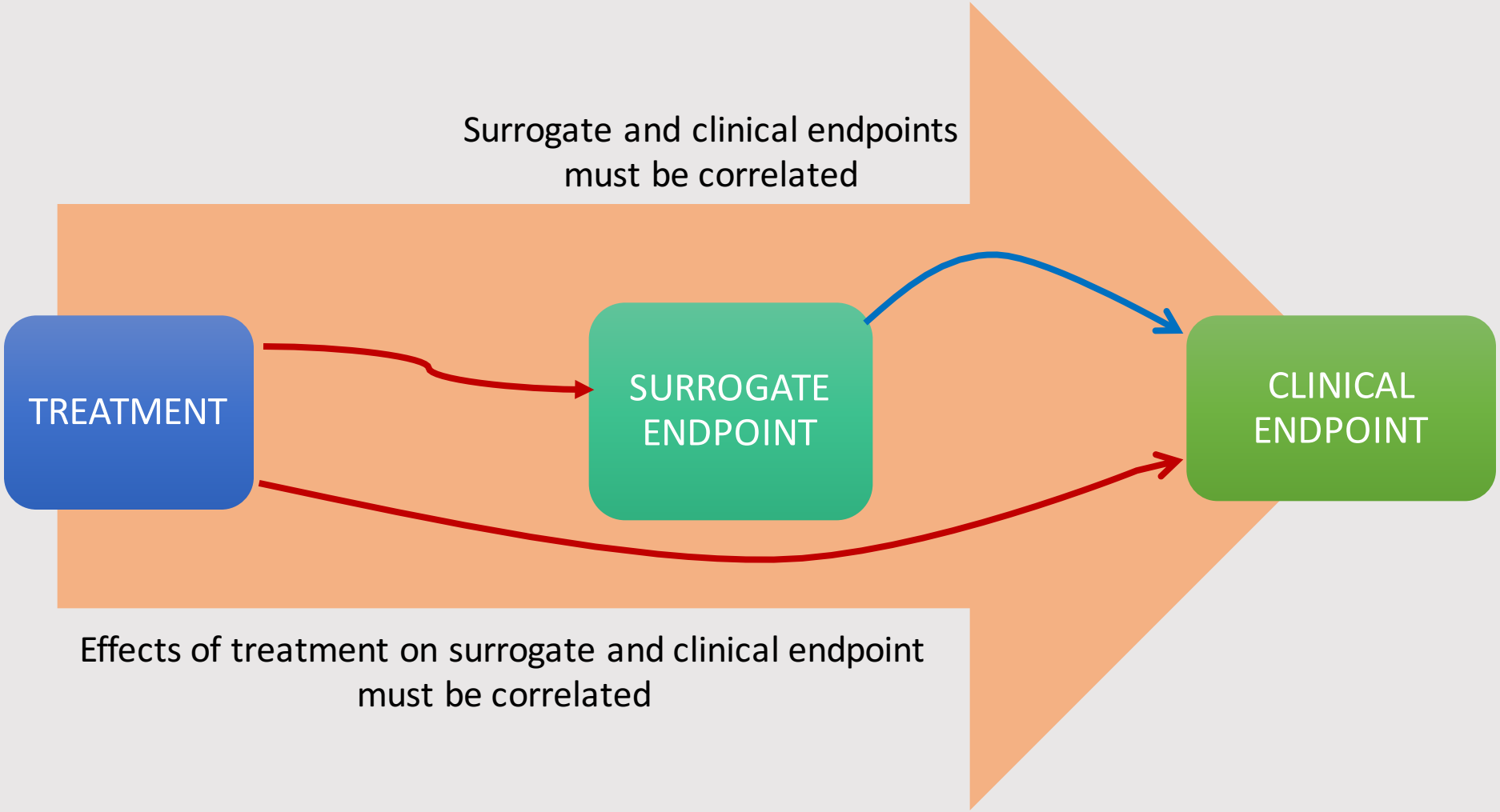

TIME
THERE IS NEW AMMUNITION IN THE WAR AGAINST CANCER.
THESE ARE THE BULLETS.
Revolutionary new pills like GLEEVEC combat cancer by targeting only the diseased cells. Is this the breakthrough we've been waiting for?


Chronic phase
CML initiation
Accelerated phase
Blastic phase
CLINICAL ENDPOINT
7-10 YEARS



Results from prospective trials suggest that imatinib therapy can be successfully discontinued in CML patients with deep and sustained molecular responses (Lancet Oncology 2010;11:1029, Blood 2013;122:515)

VALIDATION of SURROGATE ENDPOINTS



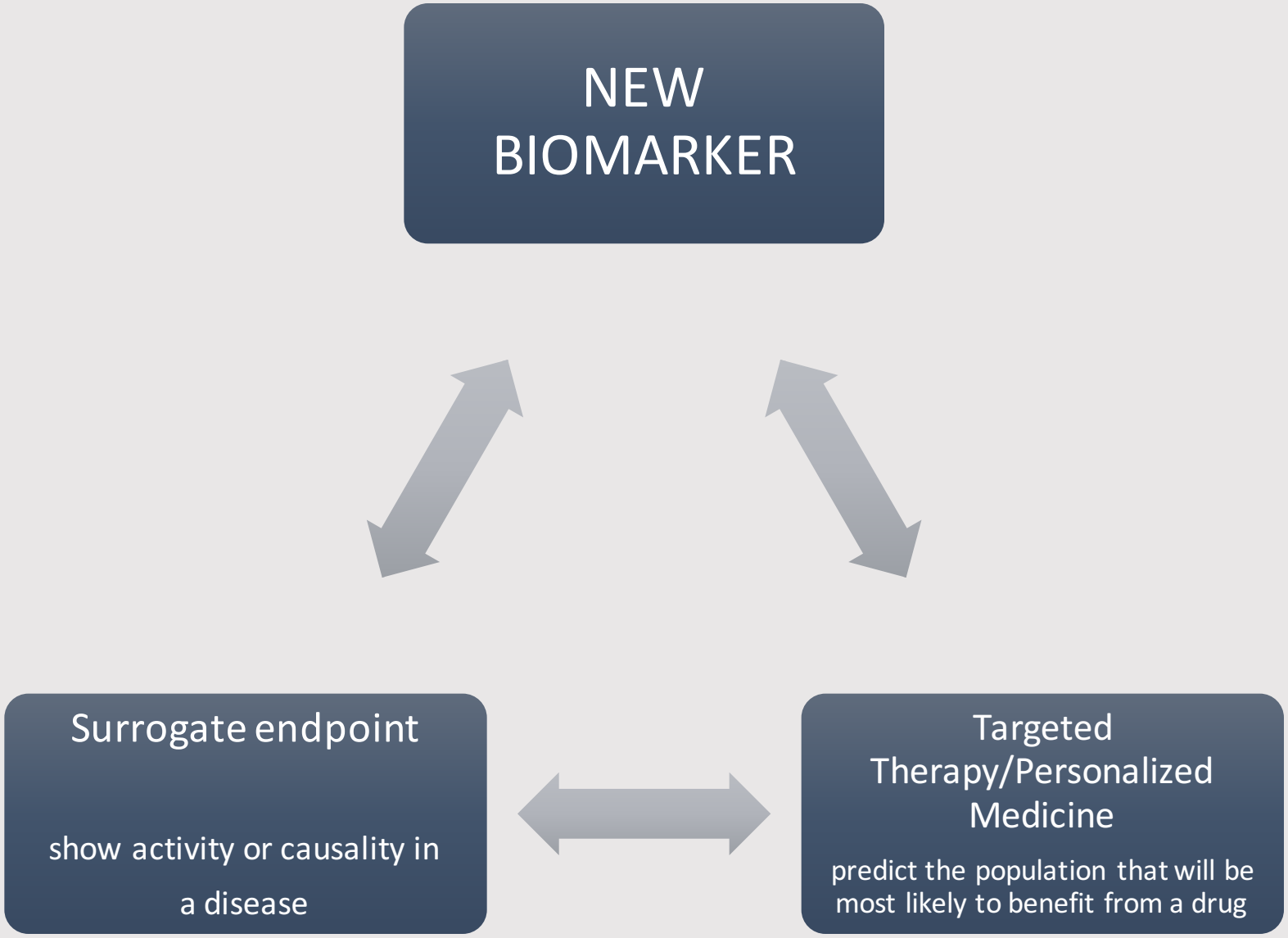
- **One-third of cancer drugs approved in the recent years come to market one the basis of improvement in overall survival, while two-thirds are approved based on a a surrogate endpoint.**

Mailankody S, Prasad V. Overall Survival in Cancer Drug Trials as a New Surrogate End Point for Overall Survival in the Real World. JAMA Oncol. 2017;3(7):889-890.

- **Not only targeted therapies but also traditional diseases benefit form surrogate endpoints:**

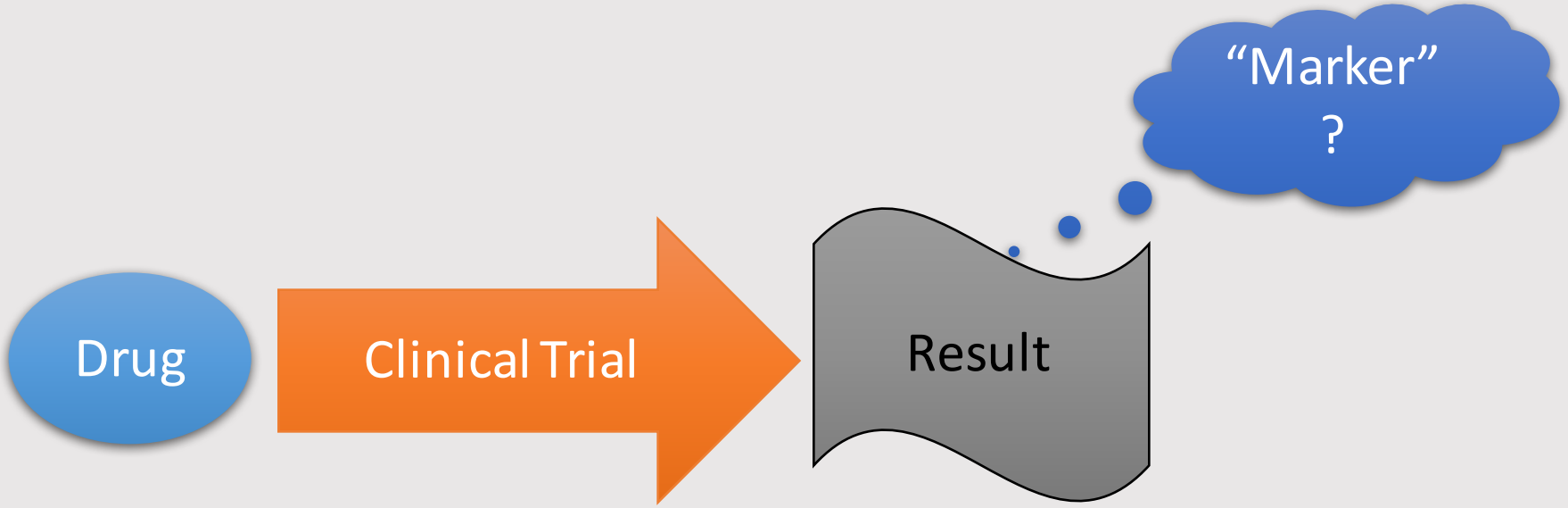
Diabetes Mellitus and HbA1c

NEW BIOMARKERS


NEW BIOMARKER
Surrogate endpoint
show activity or causality in a disease
Targeted Therapy/Personalized Medicine
predict the population that will be most likely to benefit from a drug

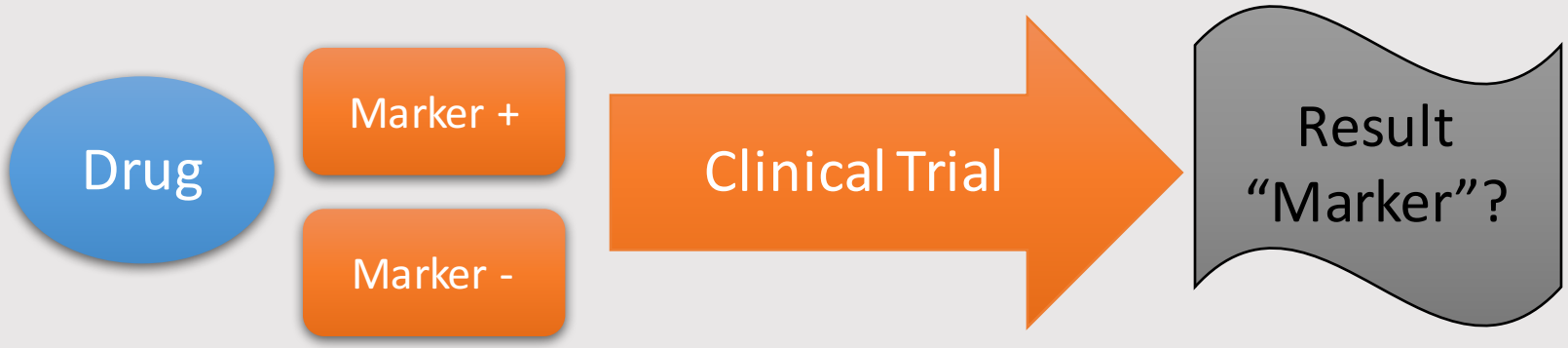
FINDING THE APPROPRIATE BIOMARKER

- **Consequtive testing strategy: First find the drug, then the biomarker**



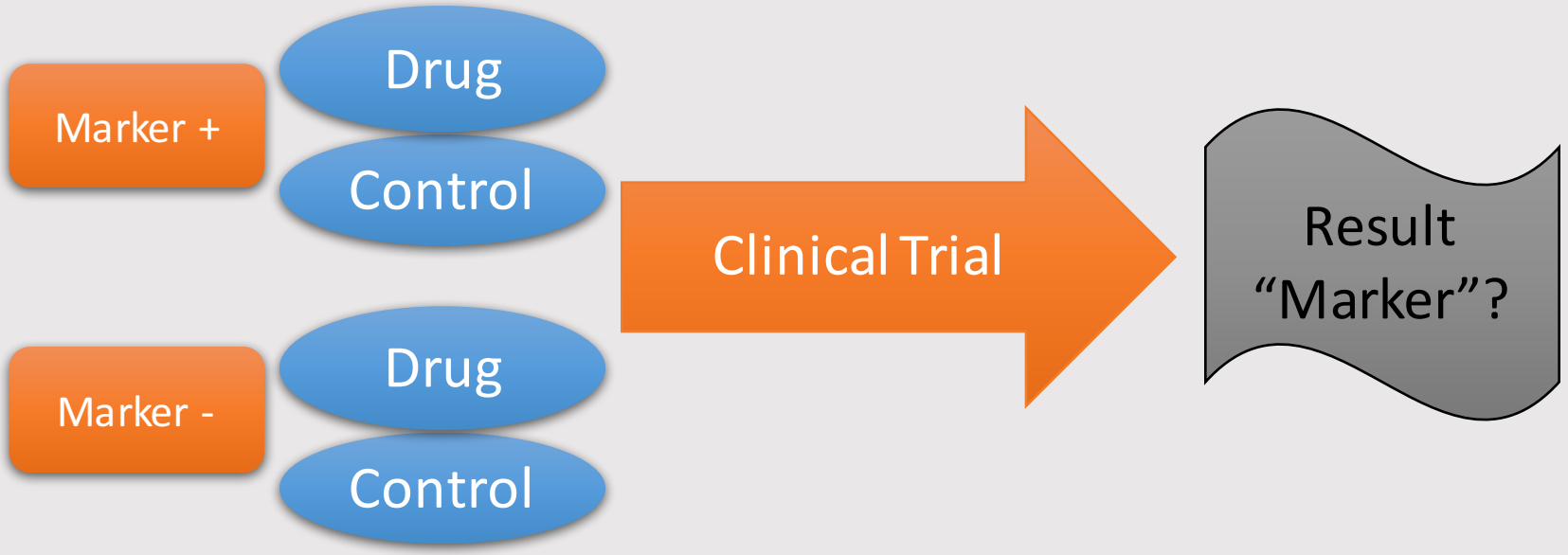
Biomarkers in Clinical Research - 1

- **Biomarker as a stratification parameter**



Biomarkers in Clinical Research - 2

- **Biomarker as a randomization strategy**



Biomarkers in Clinical Research - 3

- **Biomarker as a target**

Nilotinib + Pegylated Interferon Alpha 2a for Untreated Chronic Phase Chronic Myelogenous Leukemia (NILOPEG)

Primary Outcome Measures:

- Cumulative incidence of complete molecular remissions after 12 months of treatment with nilotinib + Pegylated Interferon (PEG-IFN) [Time Frame: 24 months] [Designated as safety issue: Yes]

Hyper CVAD Plus Ofatumumab in CD - 20 Positive Acute Lymphoblastic Leukemia (ALL)

Inclusion Criteria:

1. Patients of all ages with newly diagnosed, previously untreated CD-20+ ALL, or lymphoblastic lymphoma, Burkitt Leukemia/Lymphoma or having achieved CR with one course of induction chemotherapy.
2. Failure to one induction course of chemotherapy (these patients will be analyzed separately).
3. Performance status of 0, 1, or 2.

www.clinicaltrials.gov

EVENT DRIVEN TRIALS

- The endpoint is not the DURATION of the study but an EVENT
- The power of the study depends on the observed EVENTS

- Early termination or prolongation of a study is possible

NOT

“This study will terminate on February 2019”

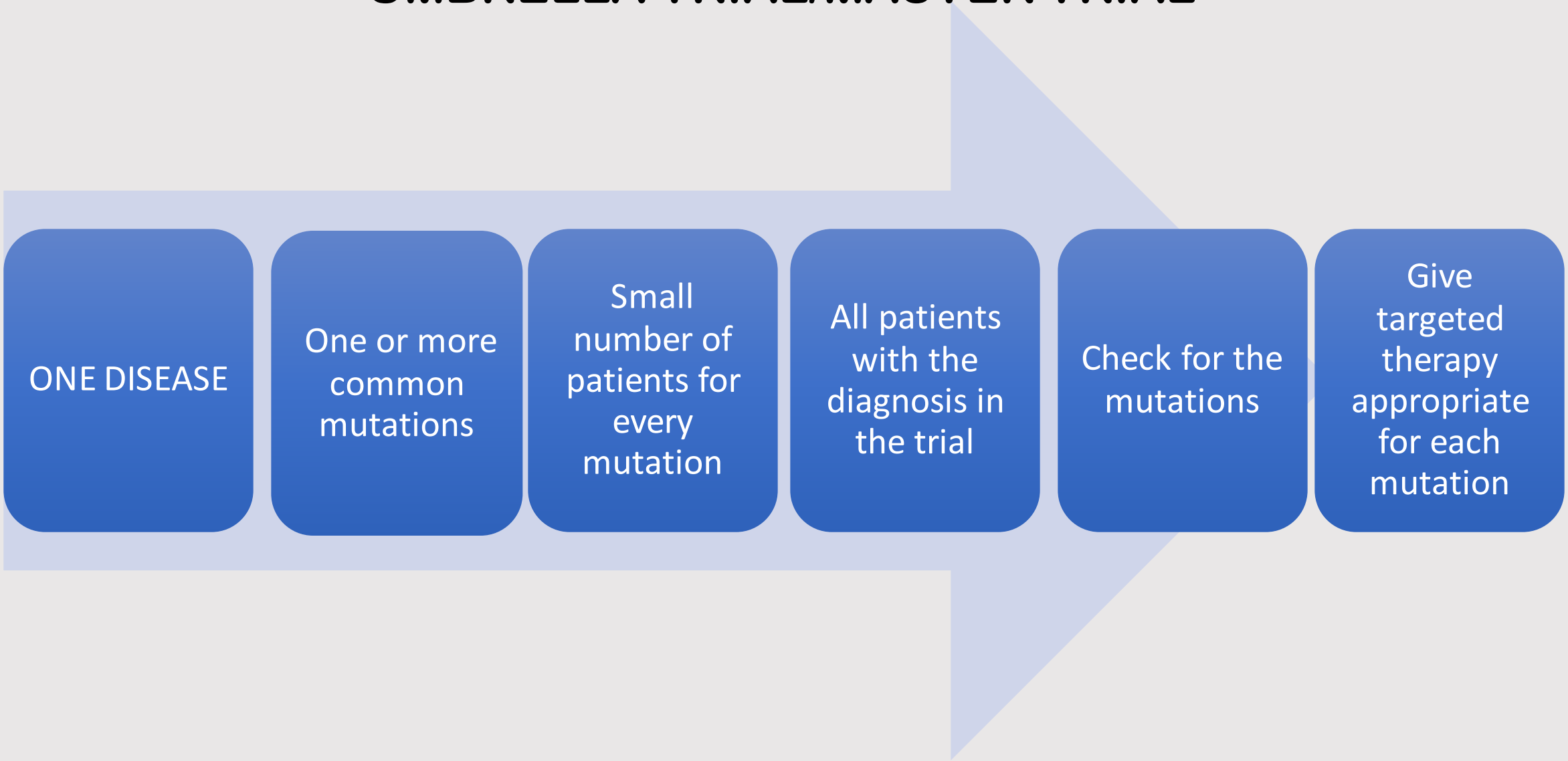
BUT

“This study will terminate after the observation of 120 EVENTS”

UMBRELLA TRIALS

BASKET TRIALS

UMBRELLA TRIAL/MASTER TRIAL



Any success in Phase II directly proceeds to Phase III in the same patients

SINGLE DIAGNOSIS
MULTIPLE
MUTATIONS

Clin Cancer Res. 2015 Apr 1;21(7):1514-24. doi: 10.1158/1078-0432.CCR-13-3473. Epub 2015 Feb 13.

Lung Master Protocol (Lung-MAP)-A Biomarker-Driven Protocol for Accelerati… Development of Therapies for Squamous Cell Lung Cancer: SWOG S1400.

Herbst RS[1], Gandara DR[2], Hirsch FR[3], Redman MW[4], LeBlanc M[4], Mack PC[2], Schwartz LH[5], Vokes E[6], Ramalingam SS[7], Brad… JD[8], Sparks D[9], Zhou Y[10], Miwa C[9], Miller VA[11], Yelensky R[11], Li Y[11], Allen JD[12], Sigal EV[12], Wholley D[13], Sigman CC[14], Blumenthal GM[15], Malik S[16], Kelloff GJ[17], Abrams JS[18], Blanke CD[19], Papadimitrakopoulou VA[20].

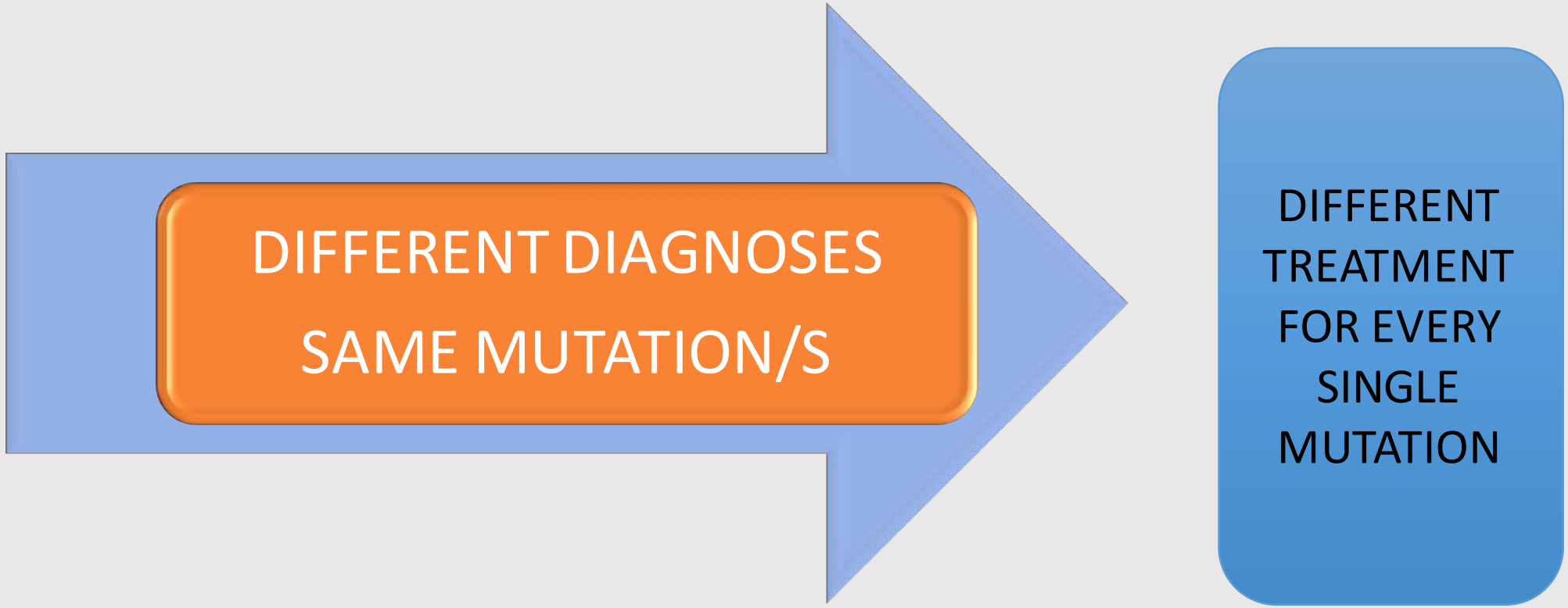
⊕ Author information

Abstract

The Lung Master Protocol (Lung-MAP, S1400) is a groundbreaking clinical trial designed to advance the efficient development of targeted therapies for squamous cell carcinoma (SCC) of the lung. There are no approved targeted therapies specific to advanced lung SCC, although The Cancer Genome Atlas project and similar studies have detected a significant number of somatic gene mutations/amplifications in lung SCC, some of which are targetable by investigational agents. However, the frequency of these changes is low (5%-20%), making recruitment and study conduct challenging in the traditional clinical trial setting. Here, we describe our approach to development of a biomarker-driven phase II/II multisubstudy "Master Protocol," using a common platform (next-generation DNA sequencing) to identify actionable molecular abnormalities, followed by randomization to the relevant targeted therapy versus standard of care.

ALL IN A BASKET

BASKET TRIALS


DIFFERENT DIAGNOSES
SAME MUTATION/S
DIFFERENT TREATMENT FOR EVERY SINGLE MUTATION

NCI-MATCH: Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors or Lymphomas

Condition	Intervention	Phase
Advanced Malignant Neoplasm Lymphoma Refractory Malignant Neoplasm Solid Neoplasm	Drug: Afatinib Drug: Akt inhibitor AZD5363 Drug: Binimetinib Drug: Crizotinib Other: Cytology Specimen Collection Procedure Drug: Dabrafenib Drug: Dasatinib Drug: Defactinib Drug: FGFR Inhibitor AZD4547 Other: Laboratory Biomarker Analysis Biological: Nivolumab Drug: Osimertinib Drug: Palbociclib Drug: PI3K-beta Inhibitor GSK2636771 Drug: Sunitinib Malate Drug: Taselisib Drug: Trametinib Biological: Trastuzumab Emtansine Drug: Vismodegib	Phase 2

DIFFERENT DIAGNOSES
SAME MUTATION/S

VOLUME 33 · NUMBER 9 · MARCH 20 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Molecular Profiling and Targeted Therapy for Advanced Thoracic Malignancies: A Biomarker-Derived, Multiarm, Multihistology Phase II Basket Trial

Ariel Lopez-Chavez, Anish Thomas, Arun Rajan, Mark Raffeld, Betsy Morrow, Ronan Kelly, Corey Allan Carter, Udayan Guha, Keith Killian, Christopher C. Lau, Zied Abdullaev, Liqiang Xi, Svetlana Pack, Paul S. Meltzer, Christopher L. Corless, Alan Sandler, Carol Beadling, Andrea W... David J. Liewehr, Seth M. Steinberg, Arlene Berman, Austin Doyle, Eva Szabo, Yisong W... and Giuseppe Giaccone

See accompanying editorial on page 975

A B S T...

Purpose
We conducted a basket clini... to independently evaluate the ... molecular aberrations in multiple histolog...

Patients and Methods
We enrolled patients with advance... (NSCLC), small-cell lung cancer, and thymic malignancies who underwe... ation of oncogenic drivers. Patients were enrolled onto a not-otherwise-specifie... ted with standard-of-care therapies or one of the following five biomarker-matched trea... groups: erlotinib for *EGFR* mutations; selumetinib for *KRAS, NRAS, HRAS,* or *BRAF* mutations; MK2206 for *PIK3CA, AKT,* or *PTEN* mutations; lapatinib for *ERBB2* mutations or amplifications; and sunitinib for *KIT* or *PDGFRA* mutations or amplification.

Results
Six hundred forty-seven patients were enrolled, and 88% had their tumors tested for at least one gene. *EGFR* mutation frequency was 22.1% in NSCLC, and erlotinib achieved a response rate of 60% (95% CI, 32.3% to 83.7%). *KRAS* mutation frequency was 24.9% in NSCLC, and selumetinib failed to achieve its primary end point, with a response rate of 11% (95% CI, 0% to 48%). Completion of accrual to all other arms was not feasible. In NSCLC, patients with *EGFR* mutations had the longest median survival (3.51 years; 95% CI, 2.89 to 5.5 years), followed by those with *ALK* rearrangements (2.94 years; 95% CI, 1.66 to 4.61 years), those with *KRAS* mutations (2.3 years; 95% CI, 2.3 to 2.17 years), those with other genetic abnormalities (2.17 years; 95% CI, 1.3 to 2.74 years), and those without an actionable mutation (1.85 years; 95% CI, 1.61 to 2.13 years).

Conclusion
This basket trial design was not feasible for many of the arms with rare mutations, but it allowed the study of the genetics of less common malignancies.

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Support information appears at the end of this article.

A.L.-C. and A.T. contributed equally to this work.

Clinical trial information: NCT01306045.

Terms in blue are defined in the glossary, found at the end of this article

SURROGATE BIOMARKERS

DIFFERENT TUMORS

Non-small cell Lung ca
Small-cell Lung ca
Thymic malignancies

NCI-MPACT

Treatment for one of the 5 different biomarkers

Erlotinib – EGFR

Selumetinib – KRAS, NRAS..

MK2206 - PIK3CA, AKT..

Lapatinic – ERBb2

Sunitinib – KIT, PRGFRA

Standart care therapy

ADAPTIVE DESIGN

or

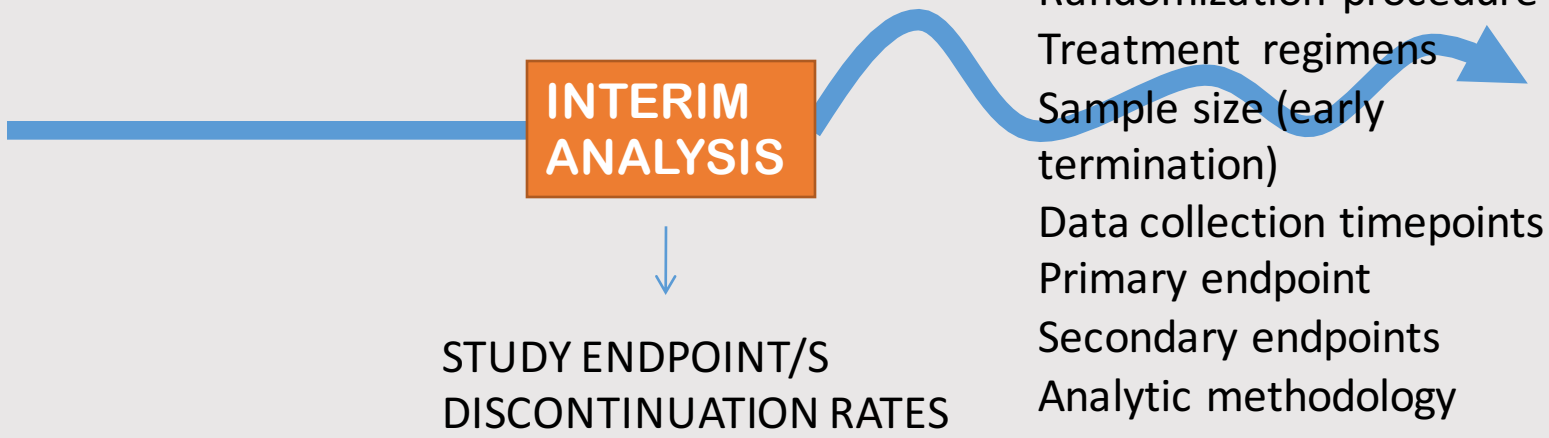
learning while walking

Modification of one or more specified aspects of the study design and hypotheses based on analysis of data during the study

Revisions Based on Information From a Study External Source is not an adaptive design

ADAPTIVE DESIGN

- Define the timepoints
- Fully blinded or unblinded analysis
- Plan revisions and adaptations after the analysis

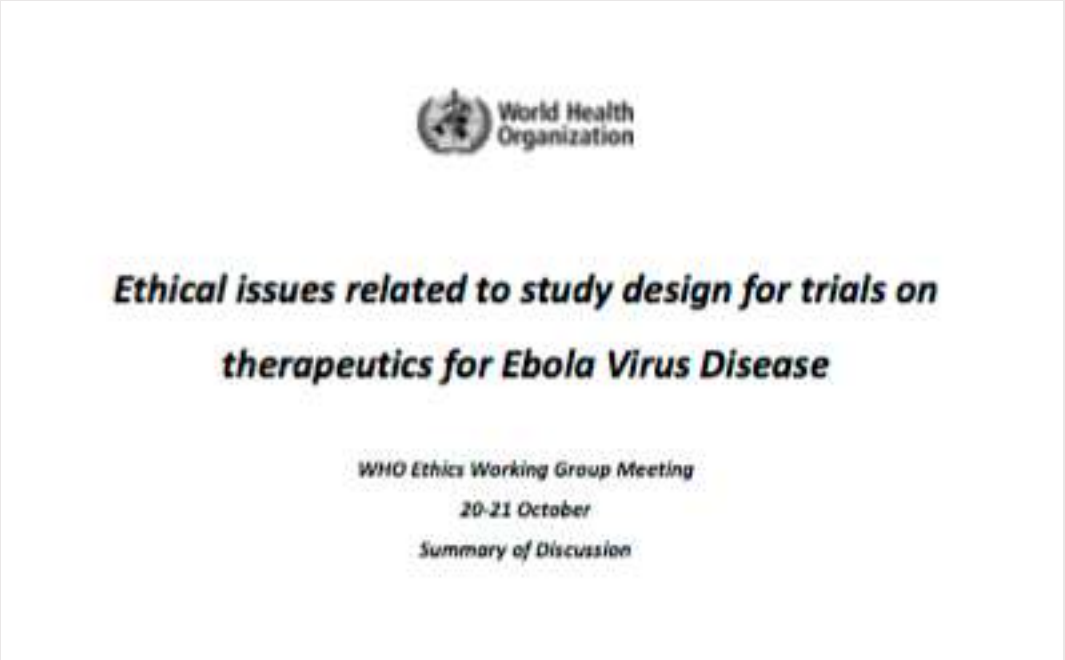


PROBLEMS

- Adaptation leading to a false conclusion that the treatment is effective – Type I error

ANALYTICAL BLINDING

INVESTIGATOR SHIELDING


World Health Organization

Ethical issues related to study design for trials on therapeutics for Ebola Virus Disease

WHO Ethics Working Group Meeting

20-21 October

Summary of Discussion

THE LANCET Global Health Blog

Evaluating Ebola interventions: adaptive designs should be commonplace

10th Oct 2014 · Ebola virus disease · Research · Clinical trials · 3 comments

ENRICHEMENT STRATEGIES

Prospective use of any patient characteristic to select a study population in which detection of a drug effect) is more likely than it would be in an unselected population.

Selection:

- demographic,
- pathophysiologic,
- historical,
- genetic or proteomic,
- clinical,
- psychological characteristics

CARDIOVASCULAR DISEASE

Severe cardiovascular disease (2 or more coronary artery occlusion)

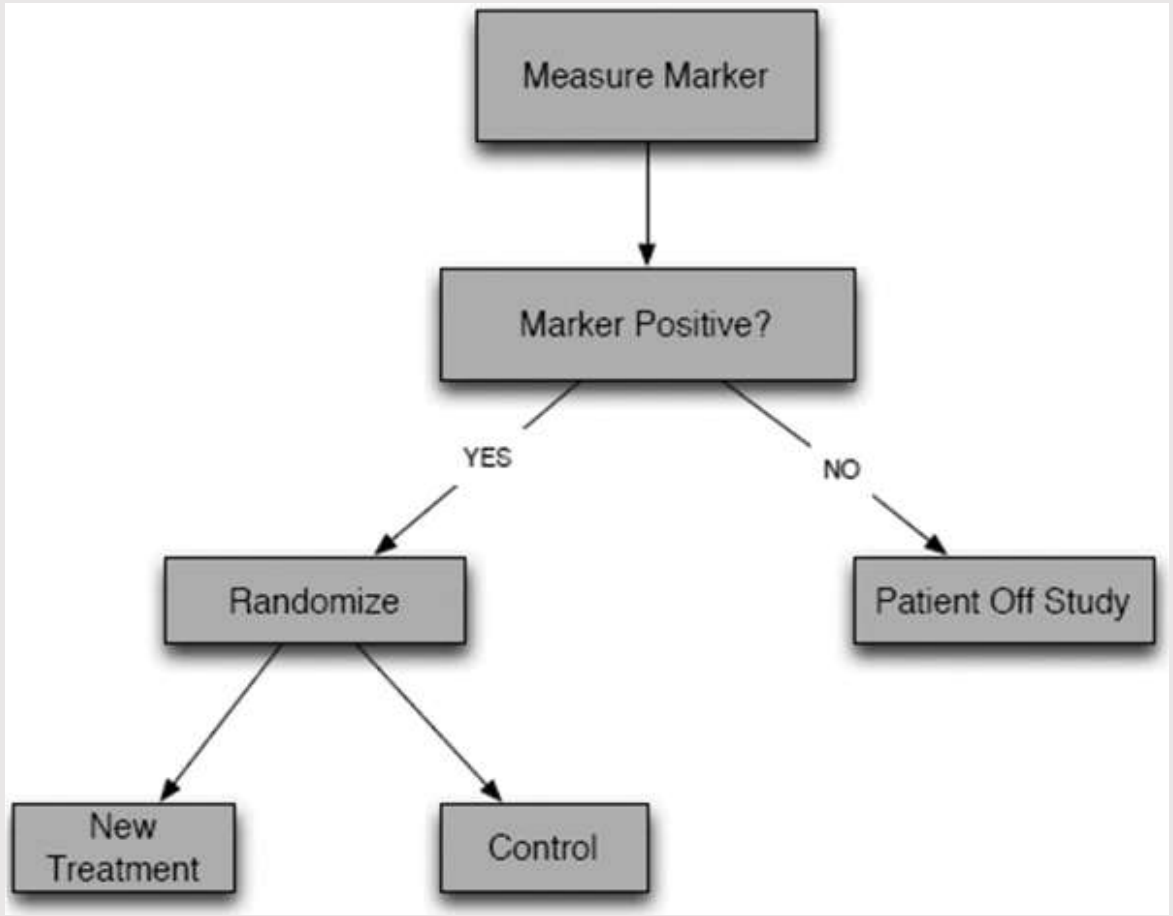
- Large study population
- Moderate or slight effect

Severity of the illness + other factors that can indicate increased risk:

- **history of recent myocardial infarction or stroke;**
- **the presence of concomitant illness such as diabetes, hypertension, or hyperlipidemia;**
- **very high LDL cholesterol, low HDL cholesterol and high C-reactive protein (CRP)**

- Small study population
- Distinctive effect

considerably reduces the sample size (the enalapril and statin trials)


Measure Marker
Marker Positive?
YES
NO
Randomize
Patient Off Study
New Treatment
Control

1. USING DIFFERENT/SURROGATE END POINT/S
2. DEVELOPING NEW BIOMARKERS
3. PUTTING ALL IN A BASKET
4. ADAPTIVE DESIGN
5. ENRICHEMENT STRATEGIES
6. **REAL LIFE DATA (BIG DATA)**

REFLECTING REAL LIFE

Mega –Trials: Clinical Research conducted on more than 10.000 participants

- HIGH BUDGET
- LONG TERM
- NEEDS DETAILED ORGANISATION
- NEW APPROACHES SUCH AS VIRTUAL or RISK BASED MONITORIZATION

Really reflects real life?

REAL LIFE DATA – BIG DATA

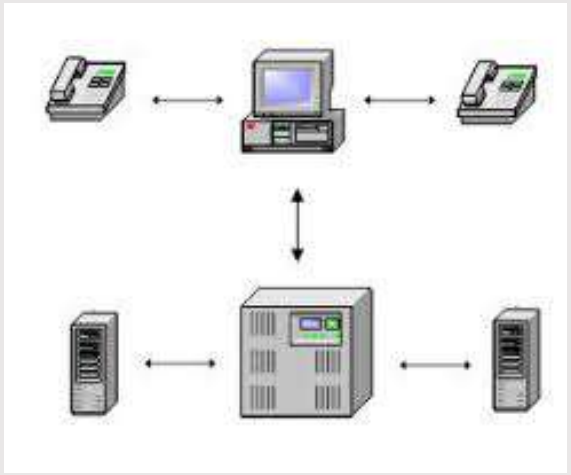
- **Data Base:** Cross-sectional and horizontal data
- **Surveys of patients and society:** Data for epidemiologic studies
- **Patient monitorisation records:** For studies involving patient care
- **Observations from cohort studies:** The main data for real life studies
- **Pragmatic clinical research:** Clinical research mimicking real life: debatable
- **Disease registries:** Continuous recording and evaluation of specific indications in specific center/centers

PROBLEMS

- Lack of resources/data (countries and data)
- Low sensitivity– Ambigious diagnosis and outcome
- Missing data
- Confounding and Bias

TECHNOLOGICAL EVOLUTION

1980 1990 2000



Interactive Response Technology (IRT)

ISOLATED SYSTEMS

Clinical Trial Management Systems (CTMS),
Electronic Clinical Outcomes Assessments (eCOA)

INTEGRATED SYSTEMS

Single sign-on (SSO)
Risk-based monitoring (RBM)
Patient Engagement
eSource
Wearable devices
Electronic drug accountability

ANKARA ÜNİVERSİTESİ TIP FAKÜLTESİ
HEMATOLOJİ KLİNİK ARAŞTIRMALAR BİRİMİ

İZLEME RANDEVULARI BAŞVURU SİSTEMİ

STANDART ÇALIŞMA PROSEDÜRLERİ

İSTATİSTİKİ VERİLER

FORMLAR

Şu anda Clinicaltrials.gov'da 274416 adet çalışma yer almaktadır.

KLİNİKA V.0.0.1

Anasayfa

Mesajlar | Raporlar | Ayarlar | Çıkış

- ANASAYFA
- KULLANICI YÖNETIMI
- FIRMA ÇALIŞANLARI (0)
- FIRMALAR
- KLINIK ARAŞTIRMALAR
- BEKLEYEN RANDEVULAR (0)
- RANDEVULAR
- RANDEVU TAKVIMI
- SAHA KOORDINATÖRLERI
- DEMIRBAŞ TAKIBI

Kullanıcılar

Kullanıcılarınızı Yönetin

Firma Çalışanları (0)

Firma Çalışanlarını Yönetin

Firmalar

Firma Yönetimi

Klinik Araştırmalar

Klinik Araştırmalar Yönetimi

Randevu Takvimi

Randevu Takvimi

Onay Bekleyen Randevular (Yönetici) (0)

Merkez Onayı Bekleyen Randevular

Randevular (Saha Çalışanları)

Randevu Yönetimi

Saha Koordinatörleri

Koordinatör Yönetimi

Demirbaş Takibi

Demirbaş Yönetimi

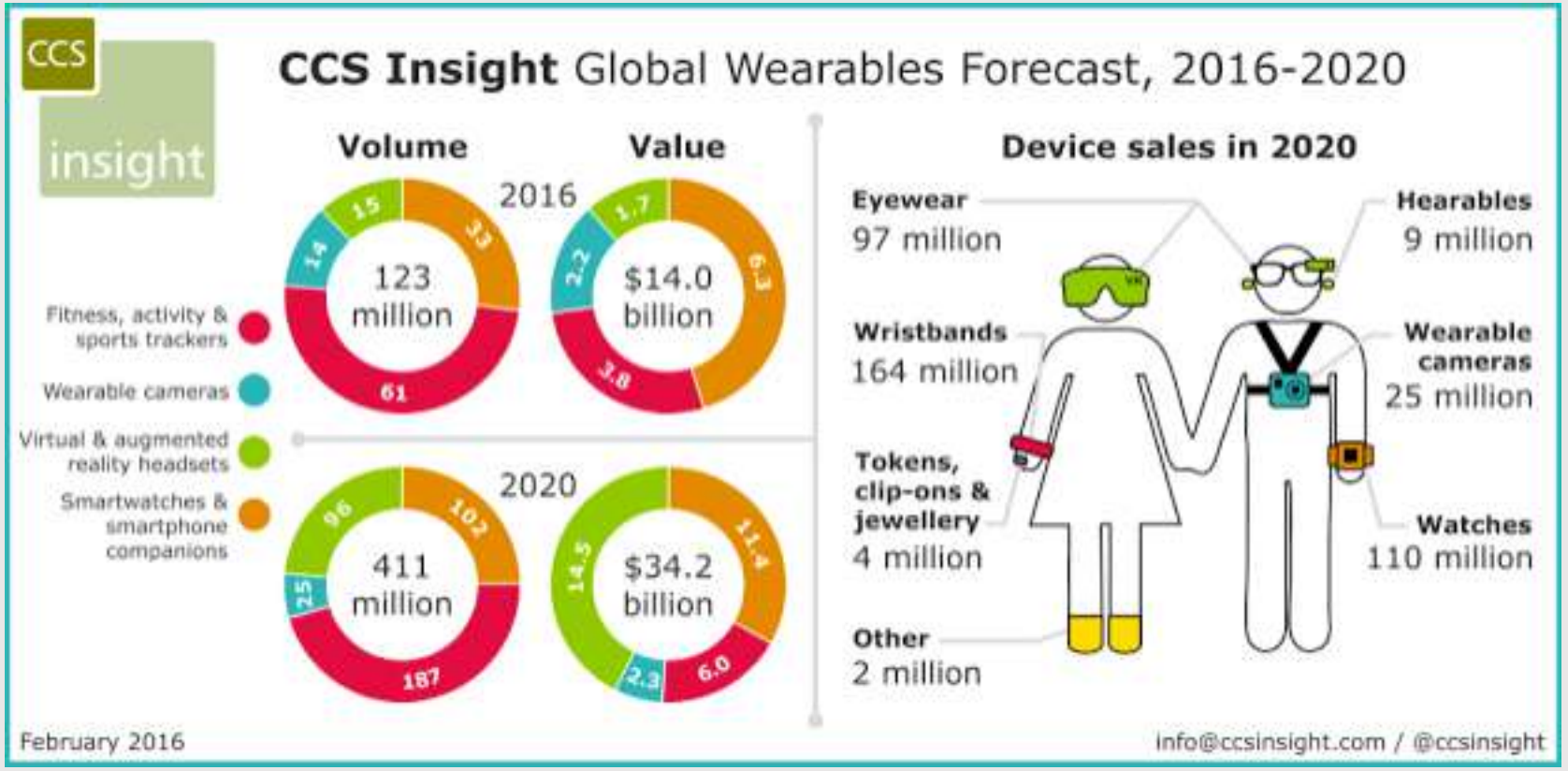
Doküman Yönetimi

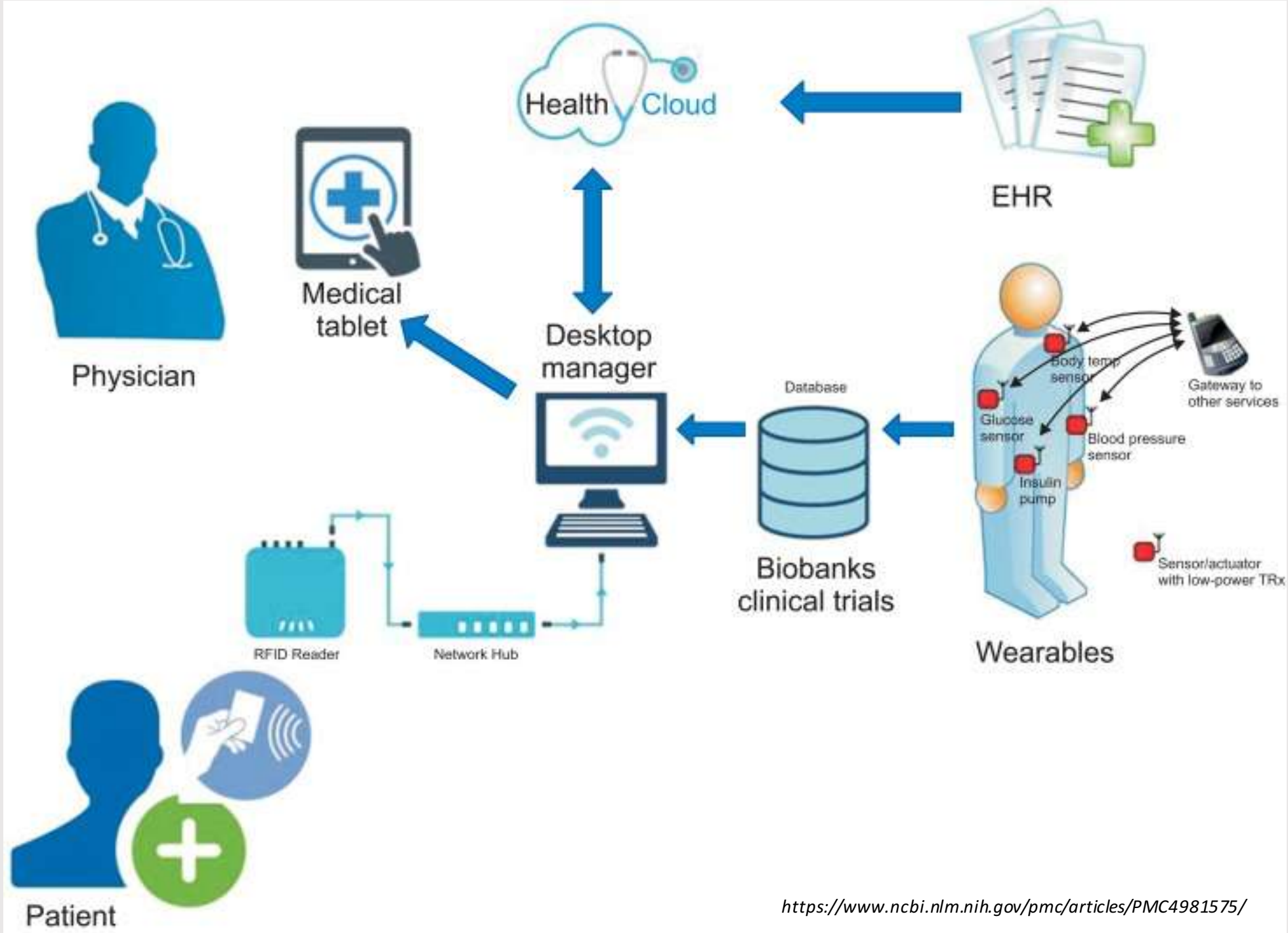
Doküman Yönetimi

Arşiv

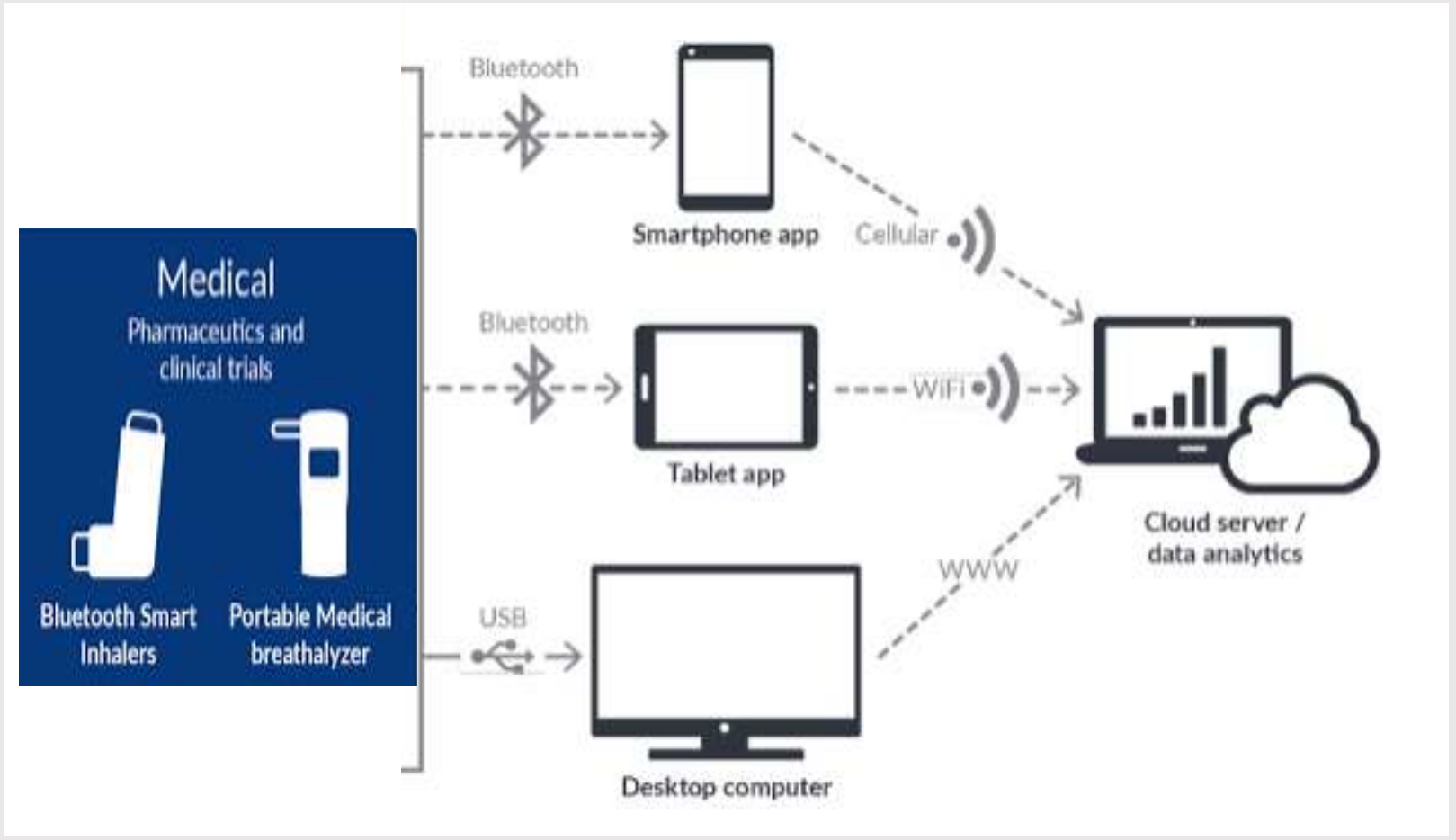
Arşiv Yönetimi

INTERNET OF THINGS

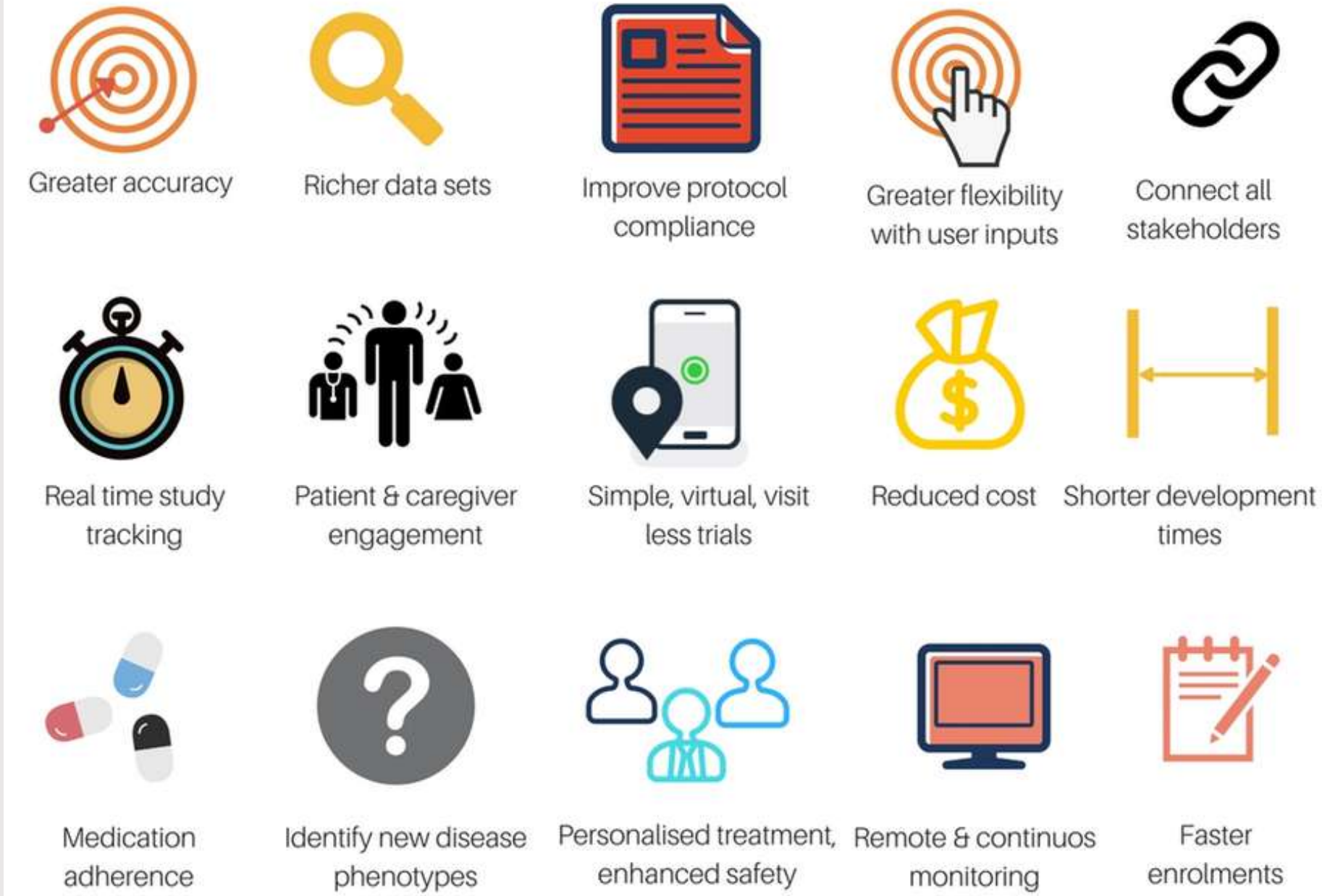




https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981575/



Applications of wearables in the fitness and clinical research context (Source: Biotaware)



https://knect365.com/clinical-trials-innovation/article/f3ebedd3-1d69-4d42-bf70-d0f8d44f7c24/internet-of-things-clinical-trials-challenges-opportunities

THANKS FOR LISTENING