Translational Research and Research Infrastructures

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Translational Research (TR)

Turning Basic Research into Medicines and Treatments

Translational Research

- The term 'translational research' first appeared in **PubMed in 1993**, sparked by the characterization of **BRCA1** and other **cancer genes**, which suggested **immediate applications** in **early detection** and **treatment of cancers**.

- The term remained low throughout the 1990s, in just a handful of papers annually, until around 2000.

Rising of Translational Research

- step **change in the scale** of investment in research,
- a **new role for the state** as scientific entrepreneur
- an **increasingly fundamental level** of investigation in **biology** and **medicine**
- **closer relationship between the laboratory and the clinic**
- accompanied by the idea of **"the therapeutic miracle"**
- **search for magic bullets** against tuberculosis, cancer, and cardiovascular disease, HIV etc.

First examples of TR

- **Cell therapy** research developed in the after WWII period as studies into the effects of **nuclear radiation** on the body and how destroyed cell systems could be repaired.
- The **stem cell in the bone marrow** and its regenerative function for the blood system, in the cases of **leukaemia patients**, were determined as biomedical **cell therapy research**

(Kraft A., 2009. Historical Studies in the Natural Sciences, 39 (2) pp: 171-218).

Wellcome Trust's definition

"Translational research helps **turn early-stage innovations into new health products**, advancing the innovation to the point where it **becomes attractive for further development** by the medical industry or healthcare agencies"

http://www.wellcome.ac.uk/funding/Innovations/wtd027704.htm

Basic Research →

Preclinical Studies→

Initial Human Testing →

Proof of Efficacy→

Proof of Effectiveness →

Industry and Health Care

Translation Research Path

This definition suggests **a one-directional flow** of information, from the laboratory into general medical care identifying the envisioned gaps between the different stages of such innovation.

The problem is **how to effectively turn new biological knowledge into widely used medical treatments.**

Translational Research (TR)

- **The one-directional model is simplistic**.

- The scientists' use of the **metaphor translation** for **flows of knowledge and information** across disciplines and their peculiar languages and practices

Translational Research (TR)

Translation is a key concept presenting the main actors as attempting to create a **central network** of **interactions** that each actor has an interest in building and defending.

The bi-directional feed back loop: bench to bedside to bench

Translational Research (TR)

- This description points out that the flow of information and what is needed to achieve **biomedical innovation** is not from the bench to the bedside but a **more complex interweaving** of stages in which complexity is reduced and then reintroduced again.

(Callon et al. 2009).

The case of Aspirin

Reference should be made to 'Aspirin' [acetylsalicylic acid (ASA)] and the fact that **it's functioning mechanisms** have only relatively recently been discovered although it has been in use **since 1500BC** when an infusion of dried myrtle leaves (which contain salicylic acid) was used to relieve back pain and **since 1899** under the trade name 'Aspirin'.

The Case of Aspirin

- **Lab knowledge**: *acetylsalicylic acid inhibits prostaglandin synthesis.*
- **Accepted clinical practice**: *aspirin administration after MI (Myocardial Infarction)*
- **Ultimate Health gain**: *decreased mortality*

Zone of Translation

- *Does aspirin decrease platelet aggregation in vivo via inhibition of prostaglandin synthesis?*
- Basic research, preclinical studies
- *Can aspirin inhibited platelet aggregation be used to prevent post MI thrombosis?*
- Clinical Trials to examine safety and efficacy.

Zone of Translation

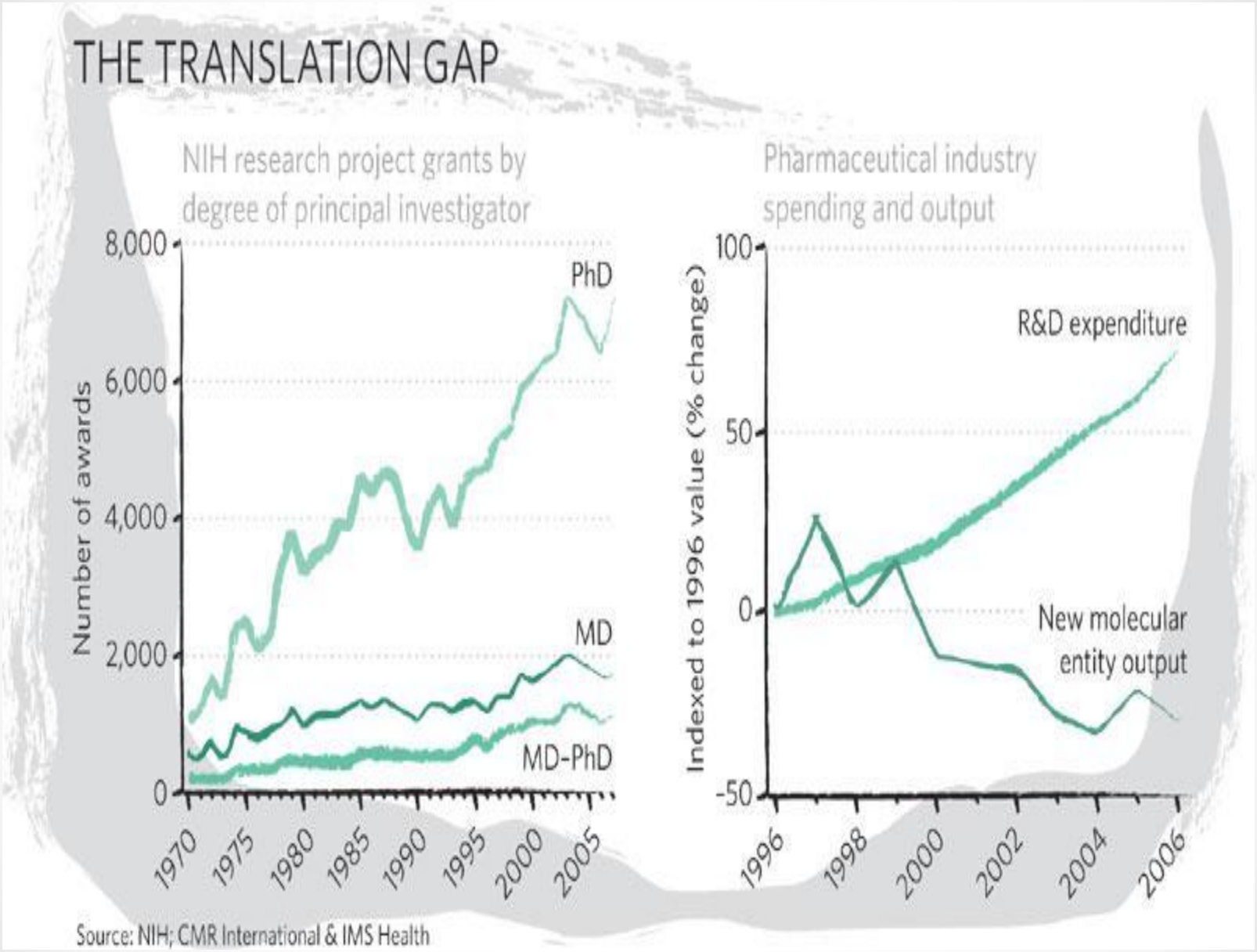
- Aspirin effectively decreases thrombosis and decreases mortality in individual patients
- *Implementation and adoption in clinical practice*.

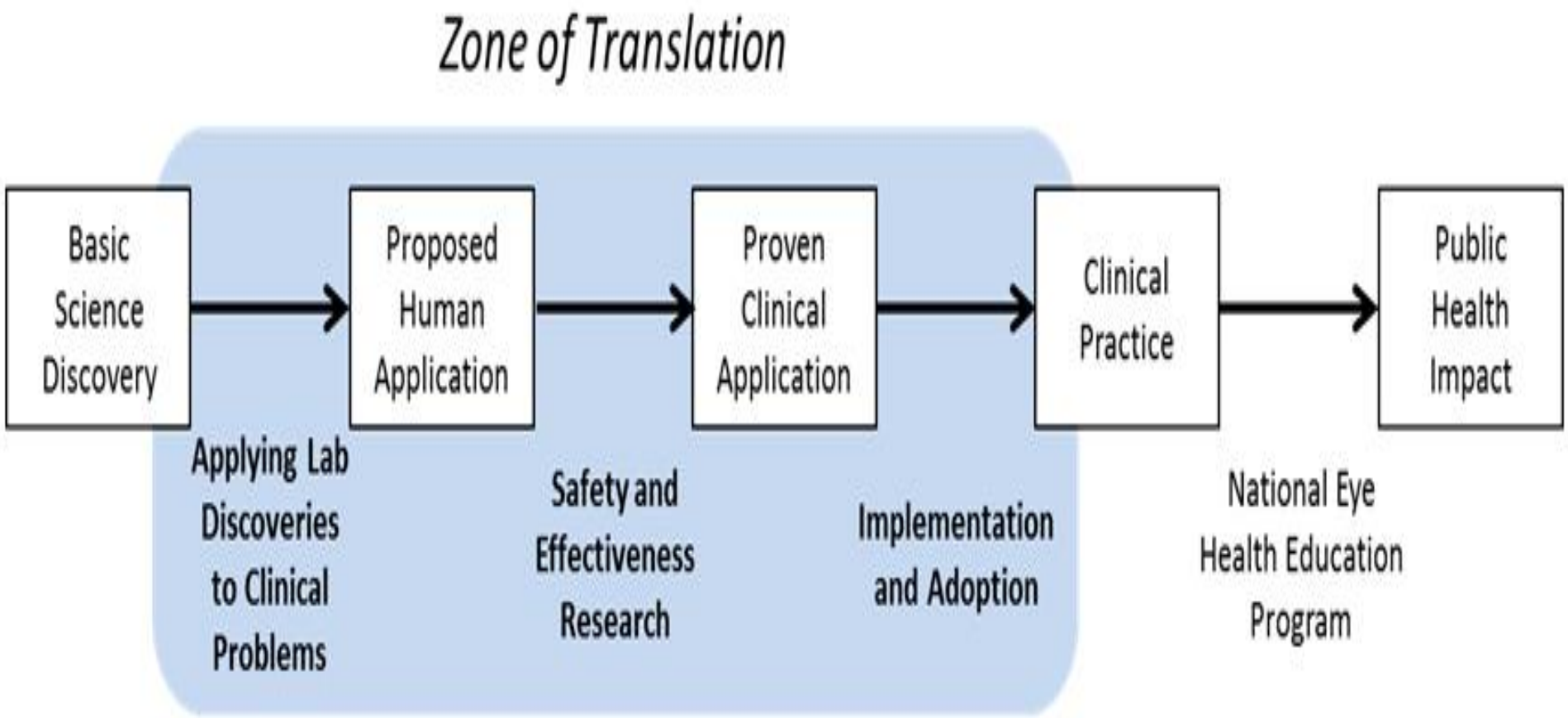
- *Does use of aspirin after MI decrease morbidity and mortality in the population?*
- **Public Health Impact**

Out of the comfort zone

- Basic scientists have **few incentives to move outside their comfort zone**.
- It means getting involved with **complex** regulatory and patent issues.
- There is risk of **career damage** to boot, because it is not the sort of research that gets published by the top journals and spurs promotion.

Translational research: Crossing the valley of death


THE TRANSLATION GAP
NIH research project grants by degree of principal investigator
Number of awards
8,000
6,000
4,000
2,000
0
PhD
MD
MD-PhD
1970
1975
1980
1985
1990
1995
2000
2005
Pharmaceutical industry spending and output
Indexed to 1996 value (% change)
100
50
0
-50
R&D expenditure
New molecular entity output
1996
1998
2000
2002
2004
2006
Source: NIH; CMR International & IMS Health


Zone of Translation
Basic Science Discovery
Proposed Human Application
Proven Clinical Application
Clinical Practice
Public Health Impact
Applying Lab Discoveries to Clinical Problems
Safety and Effectiveness Research
Implementation and Adoption
National Eye Health Education Program

Translational Research : an industrial perspective

1. **Cut backs** of internal research and development jobs in the western hemisphere (Europe and USA)

2. Following the **market growth** potential of Asia

3. '**Early innovation hunting**' with an opening of the pharmaceutical companies towards very early innovation sources within academia and small startup companies.

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Translational Research : an industrial perspective

Solutions:

- **Increased corporate funding,**
- **translational institutions to bridge innovation**
- **increasing sponsored collaborations**
- **technology hunting** groups for front leading **very early scientific ideas** and concepts

Even When an Idea Is Translated, It Takes a Long Time

From journal report or patent to product:

Range: 14 to 44 years
Median: 24 years

Source: Science. 321 (2008)1298

Challenges of Translational Research and the need for a dedicated infrastructure

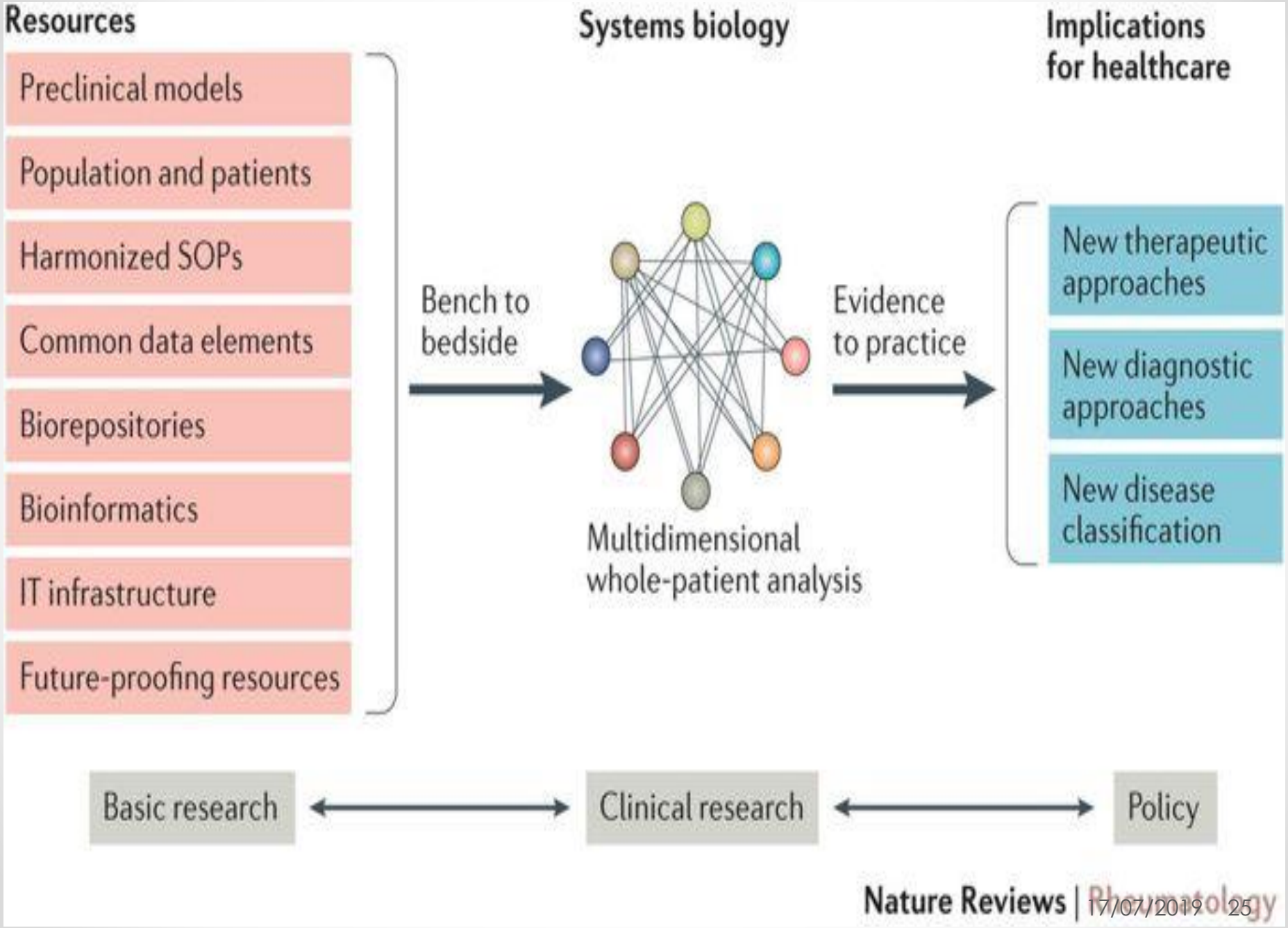
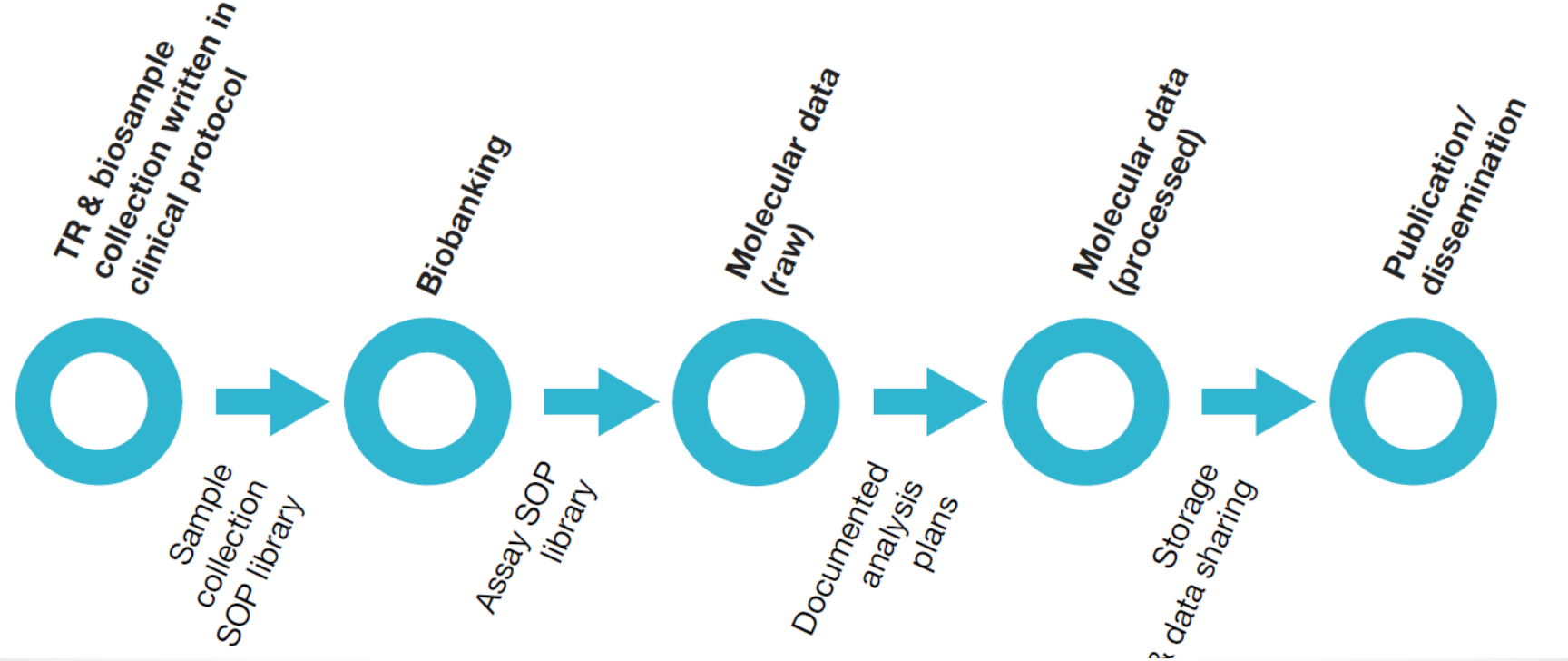

Resources
Preclinical models
Population and patients
Harmonized SOPs
Common data elements
Biorepositories
Bioinformatics
IT infrastructure
Future-proofing resources
Systems biology
Bench to bedside
Multidimensional whole-patient analysis
Evidence to practice
Implications for healthcare
New therapeutic approaches
New diagnostic approaches
New disease classification
Basic research
Clinical research
Policy
Nature Reviews | Rheumatology

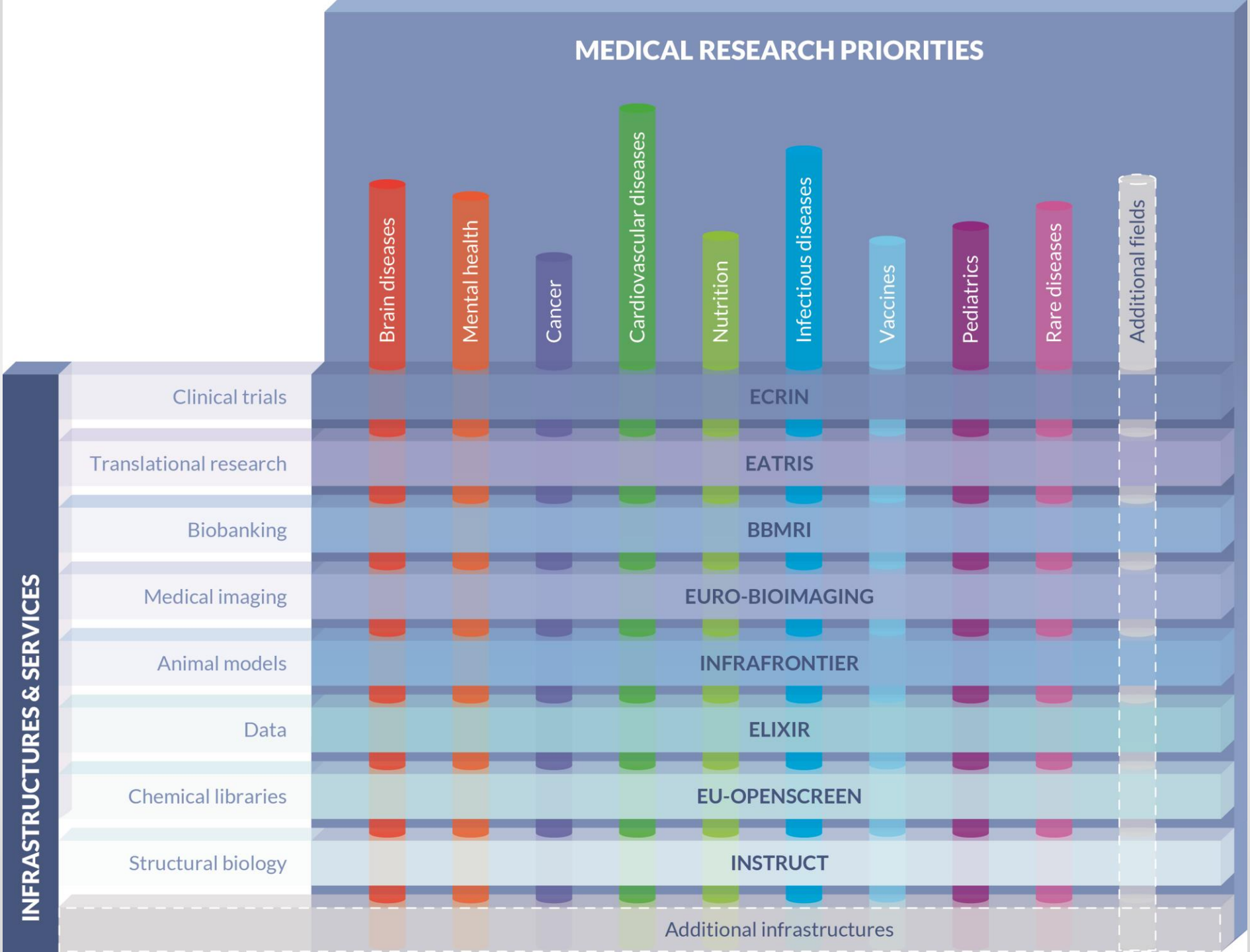
Illustration of the key elements required to establish translational research infrastructure



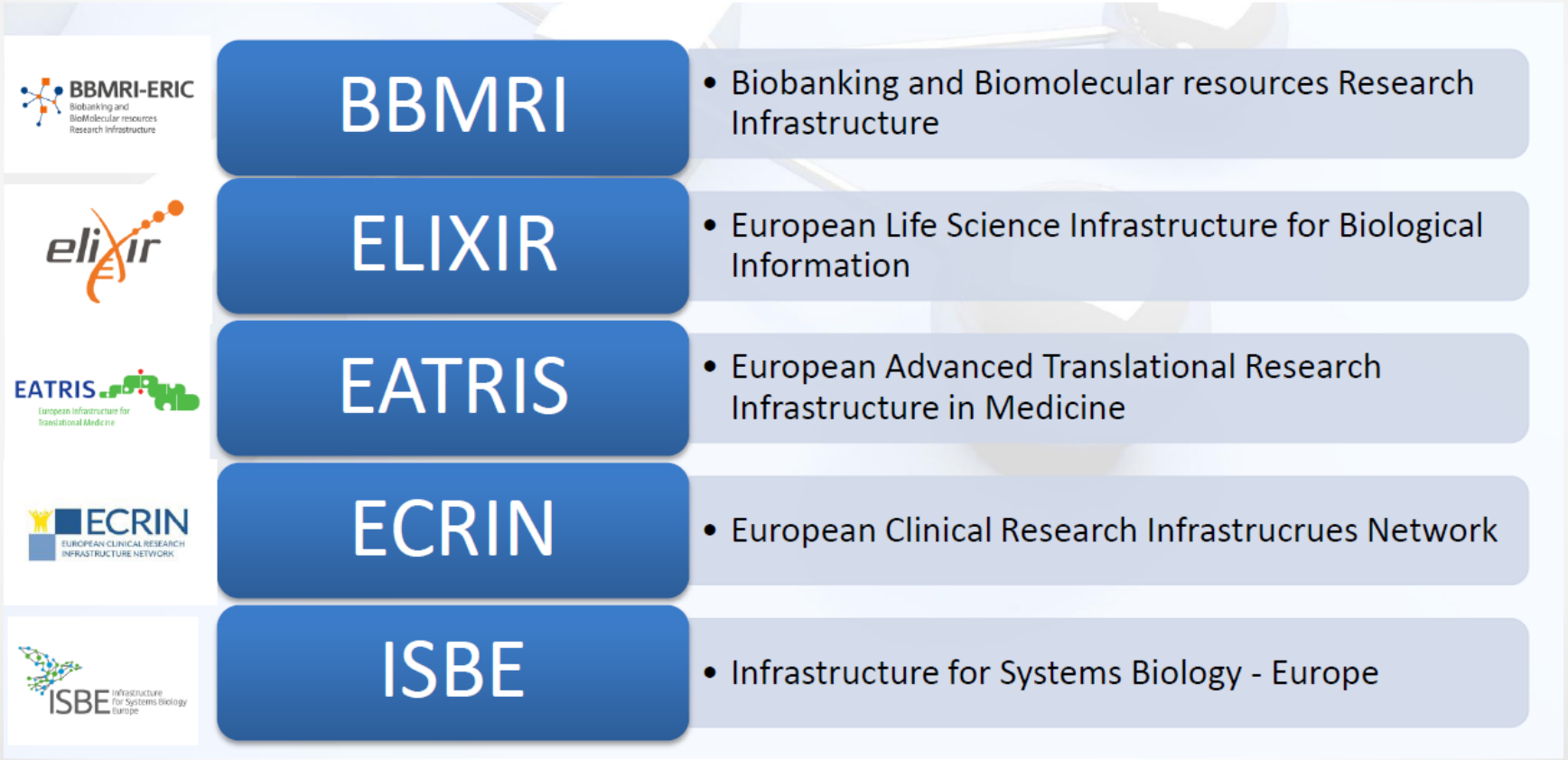
European Policy for RIs

- Research Infrastructures, including e-infrastructures, are at the **core of the knowledge triangle of research**, education and innovation and therefore play a vital role in the advancement of knowledge and technology and their exploitation.
- By offering **high quality services** to **Users** from different countries, **engaging young people**, attracting new users and preparing the **next generation of researchers**, Research Infrastructures help in structuring the scientific community and play a key role in the construction of an **efficient research and innovation environment.**
- Support to the effective and efficient construction and operation of Ris is a key priority in realizing the European Research Area and in promoting **open science and open innovation**.

Medical Research Infrastructures


MEDICAL RESEARCH PRIORITIES
Brain diseases
Mental health
Cancer
Cardiovascular diseases
Nutrition
Infectious diseases
Vaccines
Pediatrics
Rare diseases
Additional fields
INFRASTRUCTURES & SERVICES
Clinical trials
ECRIN
Translational research
EATRIS
Biobanking
BBMRI
Medical imaging
EURO-BIOIMAGING
Animal models
INFRAFRONTIER
Data
ELIXIR
Chemical libraries
EU-OPENSCREEN
Structural biology
INSTRUCT
Additional infrastructures

Relevant RIs to Translational Research



- BBMRI-ERIC
  - Involvement in Big Data initiatives (e.g. Biobank Cloud)
- ELIXIR
  - Services:
    - Archive for secure storage of human genotypic and phenotypic data
    - Registry for analysis tools
    - Catalogue of databases
    - Beacon service (for identifying datasets of interest)
    - Data management (e.g. secure archives)
    - Enables storage, copying, transfer and access of data

Translation of basic to clinical research

- BBMRI-ERIC
  - Biological sample & heath data
    - Supporting and facilitating FAIR access
  - Quality → reproducibility (ISO/TC 276, ISO/TC 212)
- ECRIN-ERIC
  - Common tools for multinational trials:
    - Disease stratification and taxonomy
    - Post-marketing follow-up observational studies
- EATRIS
  - Services:
    - Validation of biomarkers
    - Predictive in vitro/ in vivo models → reducing late stage failures
    - In vivo imaging-enabled drug development

New innovations to the market

- BBMRI-ERIC
  - Bringing together the expertise of many disciplines for biobanks and biomolecular resources to benefit health
- EATRIS-ERIC
  - Improving innovation capacity
    - Establishing public-private/ public-public collaborations
    - Support for research funders in project selection
    - Support in design and validation of novel tools (e.g. models for more predictive drug screening)
    - MoU with national regulatory agencies → research to access advice for complex cases
    - Educational curricula and workshops in translational medicine
- ECRIN-ERIC
  - Operational support for registration of clinical trials evaluating the efficacy and safety of PM strategies

Thank you for your attention!