OPEN AND RESPONSIBLE HEALTH INNOVATION

HERMANN GARDEN, STI/STP, OECD

2016 BIO FUTURE FORUM
SEOUL, KOREA

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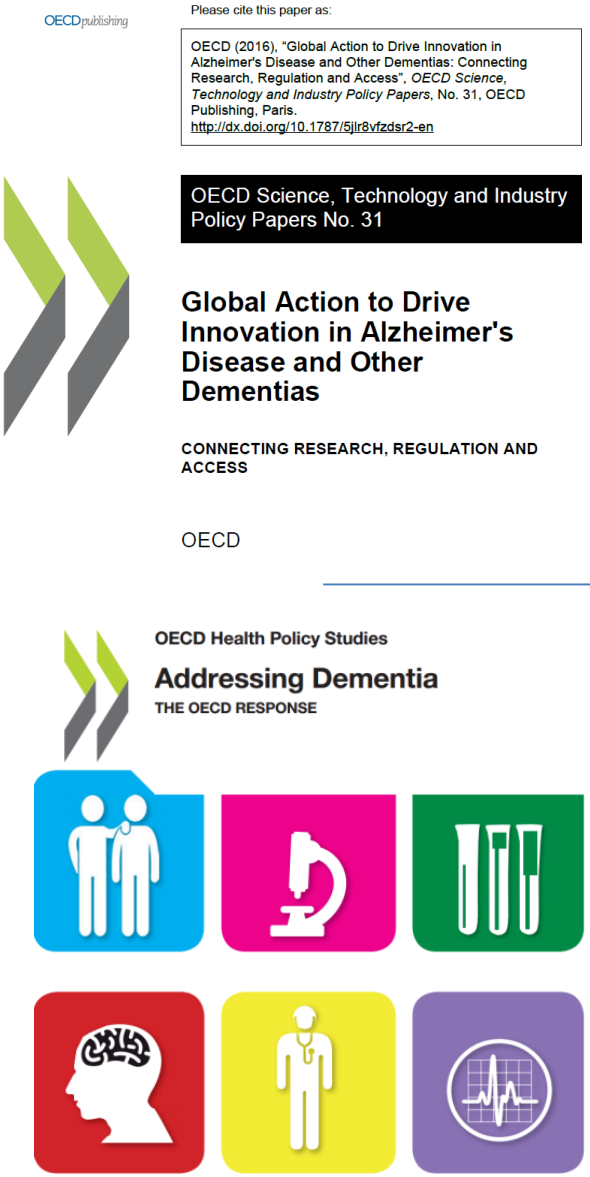
OECD publishing
Please cite this paper as:
OECD (2016), "Global Action to Drive Innovation in Alzheimer's Disease and Other Dementias: Connecting Research, Regulation and Access", OECD Science, Technology and Industry Policy Papers, No. 31, OECD Publishing, Paris.
http://dx.doi.org/10.1787/5jlr8vfzdsr2-en
OECD Science, Technology and Industry Policy Papers No. 31
Global Action to Drive Innovation in Alzheimer's Disease and Other Dementias
CONNECTING RESEARCH, REGULATION AND ACCESS
OECD


OECD publishing
Please cite this paper as:
OECD (2015), "Public-private Partnerships in Biomedical Research and Health Innovation for Alzheimer's Disease and other Dementias", OECD Science, Technology and Industry Policy Papers, No. 20, OECD Publishing, Paris.
http://dx.doi.org/10.1787/5js36rc8wwbt-en
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Public-private Partnerships in Biomedical Research and Health Innovation for Alzheimer's Disease and other Dementias
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OECD Health Policy Studies
Addressing Dementia
THE OECD RESPONSE

OECD Science, Technology and Innovation Outlook 2016
OECD

Neuron
NeuroView

CellPress

Korea Brain Initiative: Integration and Control of Brain Functions

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http://dx.doi.org/10.1016/j.neuron.2016.10.055

CellPress

Neuron
NeuroView

Neurotechnology and Society: Strengthening Responsible Innovation in Brain Science

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http://dx.doi.org/10.1016/j.neuron.2016.10.053

outline

- issues in health innovation
- opportunities in emerging technology
- integrating science, technology and society
- achieving the promise of precision medicine

issues in health innovation

Widening of the innovation gap!

R&D output does not match significant public and private investments.

- pharmaceutical industries invest 20% of revenues invested in R&D (PhRMA, 2015)
- FDA: 45 novel drug approvals in 2015; more than the average number approved annually during the past decade (FDA, 2015)
- Total global investments in public and private health R&D in 2009: USD 240 billion; 60% from business, 30% from public sector (Røttingen et al. 2013)

- We mostly treat symptoms; knowledge gaps in disease pathologies
- No new, novel drugs for psychiatric conditions developed since 60 years (Mitchell, 2015)
- Chronic disease prevalence is expected to rise by 57% by 2020 (WHO)

Widening of the innovation gap!

R&D output does not match significant public and private investments.

- National Institutes of Health (NIH, FY 2016 Request) USD 32.311 billion; incl.:

  USD 200 M Precision Med. Initiative
  USD 85 M BRAIN Initiative
  USD 350 M Alzheimer's disease
  USD 100 M AMR Initiative
- Major advances in, e.g. epigenetics, imaging technology, systems biology, synthetic biology, biomarkers etc.

- 15-20 years from scientific breakthrough to impact (Baker, 2016)
- 1 out of 10 products that enter clinical development advances to FDA approval (Hay et al. 2014)
- Global drug spending: USD 800 billion (2013), accounting for 20% of total health costs (OECD, 2015)
- US (2012): specialty drugs represent just 1% of total prescriptions but account for 25% of total spending (OECD, 2015)

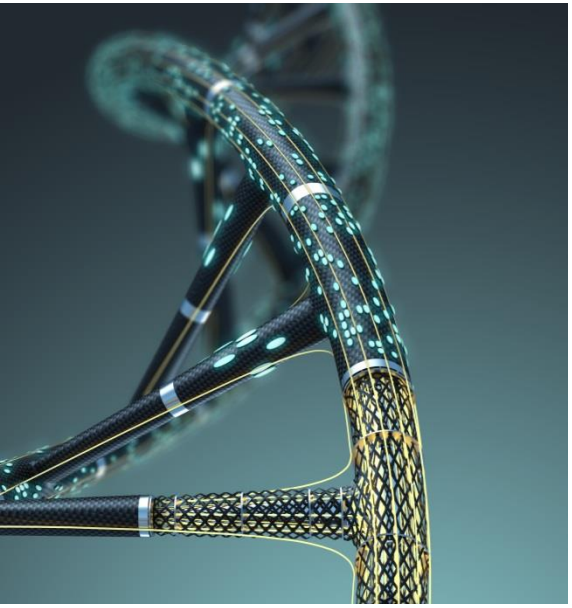
opportunities in emerging technology

opportunities in emerging technology

Policy-makers aim to:

- Anticipate the direction and impact of future products and processes.
- Find solutions for shared problems.
- Develop appropriate policies in science funding, openness and collaboration, IPRs, public engagement, and ethical, legal, social implications.

Synthetic Biology

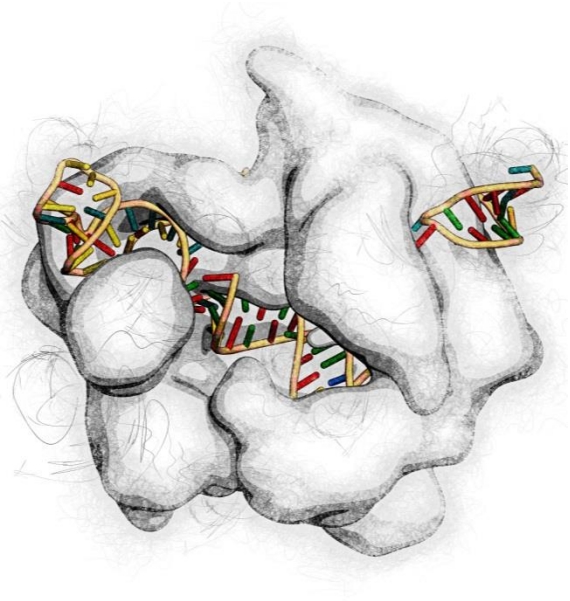


- "Design and synthesis of a minimal bacterial genome" (Hutchison et al. 2016): JCVI-syn3.0
- "A semi-synthetic organism with an expanded genetic alphabet" (Malyshev et al. 2014)
- "Synthetic biology as a source of global health innovation" (Rooke, 2013)
- "Paper-Based Synthetic Gene Networks" (Pardee et al. 2014)

Policy Issues:

- Complex and long R&D processes lead to reduced effective exclusivity periods in markets
- Regulatory science not in sync with new types of products
- "Cultural gaps" between drug and diagnostics industries
- Public concerns about synthetic life and environmental safety.

Gene Editing



- "Gene Transfer into Humans" (Rosenberg, 1990)
- "Multiplex Genome Engineering Using CRISPR /Cas Systems" (Cong et al. 2013)
- "Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with HIV" (Tebas et al. 2014)
- "The societal opportunities and challenges of genome editing" (Carroll et al. 2015)

Policy Issues:

- Ethical implications of shift from "understanding and acting on" to "designing at a molecular level"
- Avoid negative perceptions that block advances in science and health
- Manage "hype"; don't overpromise == proactive governments
- Note: disruption of regulatory definitions and frameworks
- Build and implement open science and open innovation.

Stem Cells & Regenerative Medicine

- "Embryonic Stem Cell Lines Derived from Human Blastocysts" (Thomson et al. 1998)
- "High-Dose Immunosuppressive Therapy and Autologous HALT-MS" (Nash et al. 2015)
- "Stemcell clinics - a dish called hope" (Economist, 2016)
- 2014: first advanced therapy medicinal product (ATMP) containing stem cells approved by EMA

Policy Issues:

- Heterogeneity of legal and regulatory frameworks
- Lack of guidance covering the whole R&D pathway
- Need for standardisation and validation of cell therapies
- Scale-up and manufacturing (GMP in stem cell technology?)
- Need for appropriate reimbursement models
- Note: unproven health claims.

Precision Medicine

- Molecular and biochemical profiling for applying the right dose of the right drug to the right person at the right time
- Improved effectiveness and reduced toxicity of the already available therapies
- Addressing knowledge gaps in the biological underpinnings of diseases

Policy Issues:

- Unique characteristics of precision medicine R&D: small patient populations / small clinical trials / small markets
- "Understanding and accepting that ethical, economic and epistemic barriers exist, and that culture change will be required, must be the first steps towards promoting uptake of molecularly-targeted Precision Medicine." (Lewis et al. 2014)

MICROBIOME

- "Microbiota at Work" (Ash and Mueller, 2016)
- "Microbiology: Create a global microbiome effort" (Dubilier et al. 2015)
- IHMC: http://www.human-microbiome.org/
- http://www.healthydietforhealthylife.eu/
- http://www.mynewgut.eu/

POLICY ISSUES:

- Need for standardisation and validation; establishing an evidence base for clinical efficacy and safety of food products and dietary approaches
- Clarifying terminology! What is a *healthy* microbiome?
- Cross-sectoral dialogue: convene regulators, scientists, citizens and industry – both, drugs and food.

Brain Science and Neurotechnology

- "Neurogenesis in the adult human hippocampus" (Eriksson et al. 1998)
- "The antibody aducanumab reduces Aβ plaques in Alzheimer's disease" (Sevigny et al. 2016)
- "A multi-modal parcellation of human cerebral cortex" (Glasser et la. 2016)
- "Mastering the game of Go with deep neural networks and tree search" (Silver et al. 2016)

Policy Issues:

- Brain science is now moving from the lab to an industry; need to understand standards, norms, regulation, property regimes
- Need for a future-oriented discourse about the ethical, legal and social implications in human enhancement and artificial intelligence
- What happens when we do understand the brain?
- Ensure equity and justice during commercialisation

significant potential in emerging technology

-

how to translate into better health

integrating science, technology and society

SOME GOVERNANCE TOOLS:

1. Health Technology Assessment (HTA)
2. Ethical, Legal, Social Implications (ELSI)
3. Responsible Research & Innovation (RRI)
4. Anticipatory Governance
5. Open Innovation

A new contract between science, technology and society to:

- Increase social acceptability and ethical desirability
- Avoid major environmental, ethical and social damages
- Accelerate research and innovation
- Reduce business failure; increase economic efficiency
- Ensure sustainability

1. Health Technology Assessment (HTA)

Technology Assessment (TA):

established in the 1970s in order to help governments to better anticipate the social consequences of STI.

The International Network of Agencies for Health Technology Assessment (INAHTA) defines health technology assessment (HTA) as:

"a multidisciplinary field of policy analysis which studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology".

1. Health Technology Assessment (HTA)

Safety (adverse effects)

does not imply

Efficacy (effect under ideal conditions)

Efficacy

does not imply

Effectiveness (effect under "real world" circumstances)

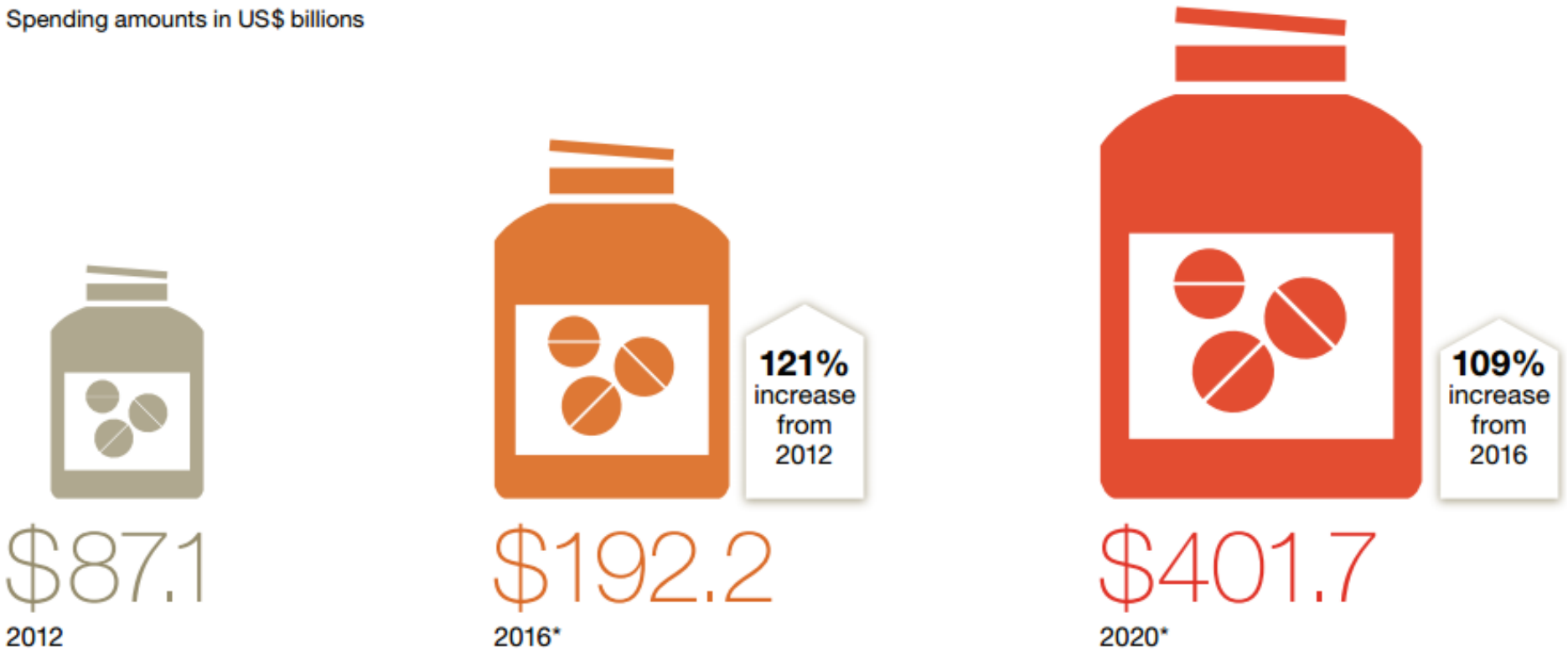
Effectiveness

does not imply

Efficiency (costs and use versus benefit)

1. Health Technology Assessment (HTA)

US specialty drug spending (PwC, 2015)



Specialty drugs are, for example, agents used to treat complex conditions; often are biologics and require special handling or delivery mechanisms.

1. Health Technology Assessment (HTA)

UK National Institute for Health and Care Excellence (NICE)

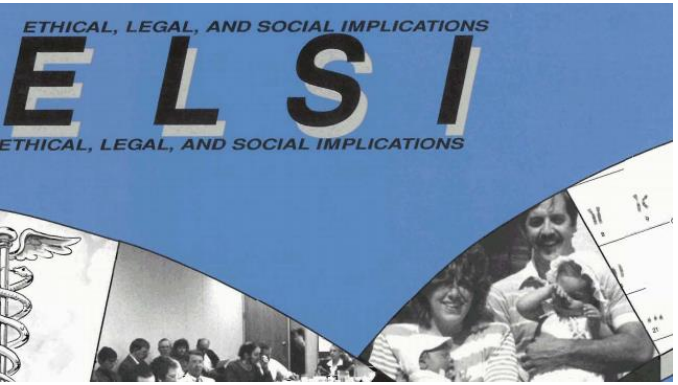
Performs technology appraisals and provides recommendations on: medicines, medical devices, diagnostics, surgical procedures, health promotion activities.

- **Clinical Evidence:** How well does a treatment work?
- **Economic Evidence:** How well does a treatment work in relation to how much it costs the National Health Service? Value for money!

Cost per QUALY (**q**uality-**a**djusted **l**ife **y**ear) = ICER (incremental cost-effectiveness ratio [pounds sterling])

ICER versus affordability! Note: issue of high-prize medicine for high prevalence diseases (e.g. Alzheimer's disease, hepatitis C).

2. Ethical, Legal, Social Implications (ELSI)



Ethical, Legal, and Social Implications (ELSI) programme was set-up in 1990 as part of the International Human Genome Project (HGP, 1990-2003).

"Traditionally, researchers in the natural sciences concentrated on their investigations and allowed society to interpret and use the results as it chose. Now for the first time a research effort includes a structure in which "hard" scientists, social scientists, health-care workers, legal experts, and philosophers discuss the implications of present and potential scientific results."
(Los Alamos Science, 1992)

2. Ethical, Legal, Social Implications (ELSI)

"21st Century Nanotechnology Research and Development Act" (US, 2003)

[108th Congress Public Law 153]
[From the U.S. Government Printing Office]
[DOCID: f:publ153.108]

[[Page 117 STAT. 1923]]

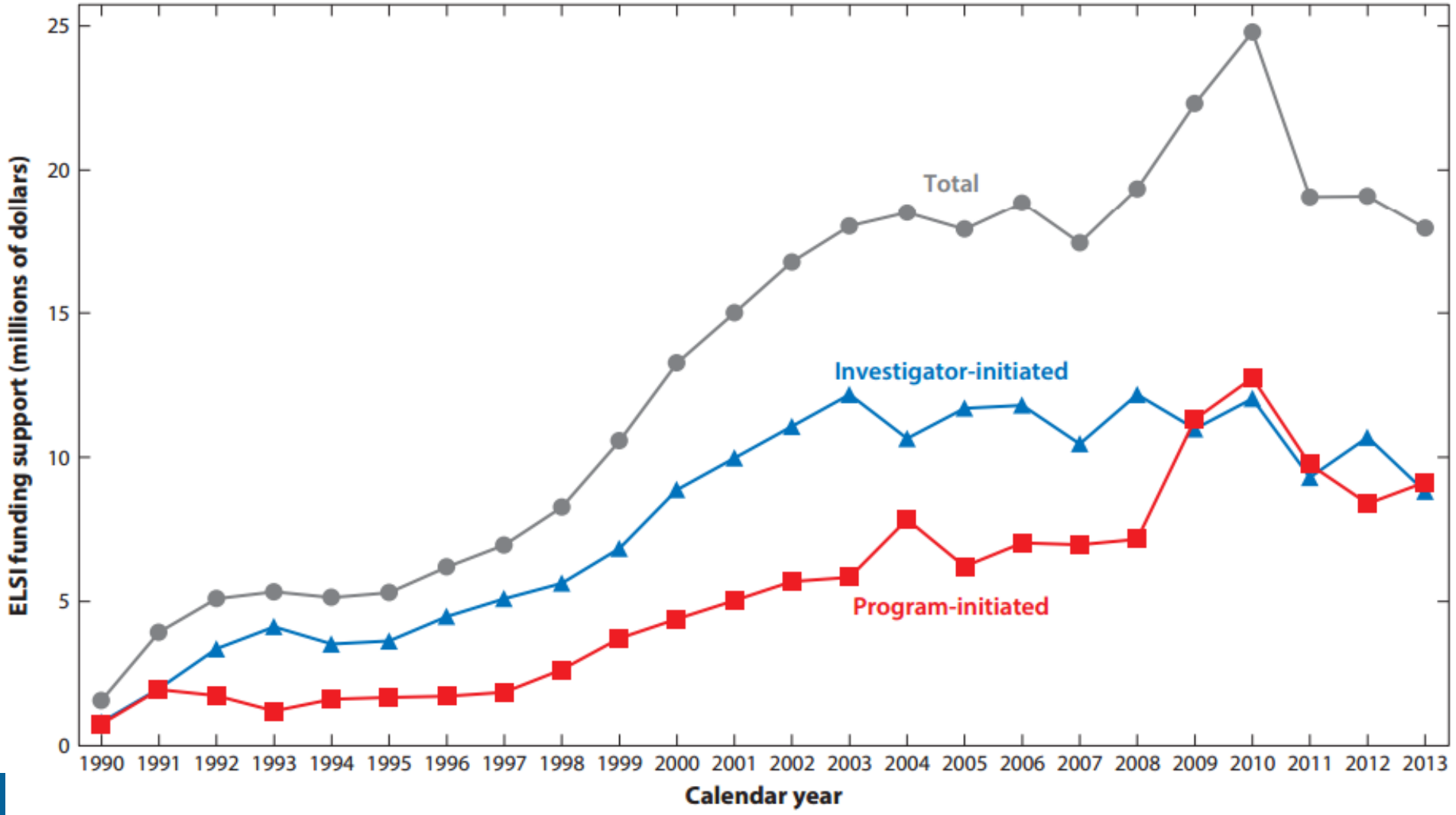
Public Law 108-153
108th Congress

Programme activities include:

- Identifying and disseminating ethical, legal and environmental issues
- Raising awareness of societal concerns in research centers
- Ensuring public input and outreach; public discussions, citizens' panels, consensus conferences, educational events
- Ensuring advances bring about improvements in quality of life for all.

2. Ethical, Legal, Social Implications (ELSI)

ELSI in genetics and genomics programme, US National Human Genome Research Institute (NHGRI) (McEwen et al. 2014)



3. Responsible Research and Innovation (RRI)

- Who benefits, how and what are the costs?
- What are the uncertainties; what happens if we are wrong?
- Who controls access to the science and the technology?

What is RRI?

"A transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) **acceptability**, **sustainability** and **social desirability** of the innovation process and its marketable products (in order to allow a proper embedding and technological advances in our society)." (Schomberg, 2013)

3. Responsible Research and Innovation (RRI)

Developing and applying RRI in Health:

European Commission: RRI forms a key action of the "Science with and for Society" objective of the EU Horizon 2020 programme.	2014 Italian Presidency of the Council of the EU: "Rome Declaration on Responsible Research and Innovation in Europe."
Nuffield Council on Bioethics, 2013: "Novel Neurotechnologies: Intervening in the Brain"	OECD Guidelines for Multinational Enterprises; responsible business conduct (OECD, 2011)

- Embedding social scientists in research labs
- Integrating societal concerns into research funding
- Developing law
- Ensuring public input and outreach

4. Anticipatory Governance

"Prediction is impossible, but anticipation of possible, plural futures is vital"

(Stilgoe et al. 2013).

Anticipatory governance has at least three components and aims:

1. Consideration of human values in deliberations about technology
2. Scenario development and foresight for a broader capacity to understand social dimensions of scientific/ technical change
3. Integration of engagement and foresight with scientific and technical work to increase the ability of natural scientists to understand the societal aspects of their own work and to inform the perspectives of social scientists on cutting-edge technology (Guston 2008).

5. Open Innovation

Open Innovation describes a move from the individual innovator to a global collective, through which researchers and business share information and use external knowledge to advance science and product development (OECD, 2008).

- Examples: Structural Genomics Consortium (SGC); McGill University, Montreal Neurological Institute (MNI); Dementia Consortium; Lilly Open Innovation Drug Discovery (OIDD)
- What are the real life experiences in Open Innovation? How to finance Open Science and Open Innovation? Do they deliver?
- Privacy risks and respects the individuals whose data are being shared (Bostrom, 2016; Economist, 2016).

achieving the promise of precision medicine

The Case of Precision Medicine (PM)

Applying new governance mechanisms. Achieving the promise of PM (1/2):

- Funders can shape the downstream trajectories of PM and ensure that mechanisms to promote responsible innovation are in place.
- Anticipatory governance would help directing the strong "technological push" of emerging technologies towards addressing pressing public health needs.
- New Teaching & training curricula help integrating Precision Medicine into the clinical environment and the wider public discourse
- Foster stakeholder participation, interdisciplinary research, pre-competitive partnerships, industry-industry collaboration, partnerships with patient organisations.

The Case of Precision Medicine (PM)

Applying new governance mechanisms. Achieving the promise of PM (2/2):

- Regulatory flexibility to cope with small target populations
- Good Genomic Practice (GGP)
- Co-development of drugs and diagnostics
- Adequate data infrastructure; interoperable datasets
- Impacts on health care costs, access and sustainability
- “Hype” and unproven health claims
- Not limiting PM to omics and gene therapy.

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