Lessons from the EHRA Innovation Summit:

How EHRA can help to clear the hurdles for getting innovative solutions reimbursed

Frits W. Prinzen PhD

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A Registered Branch of the ESC

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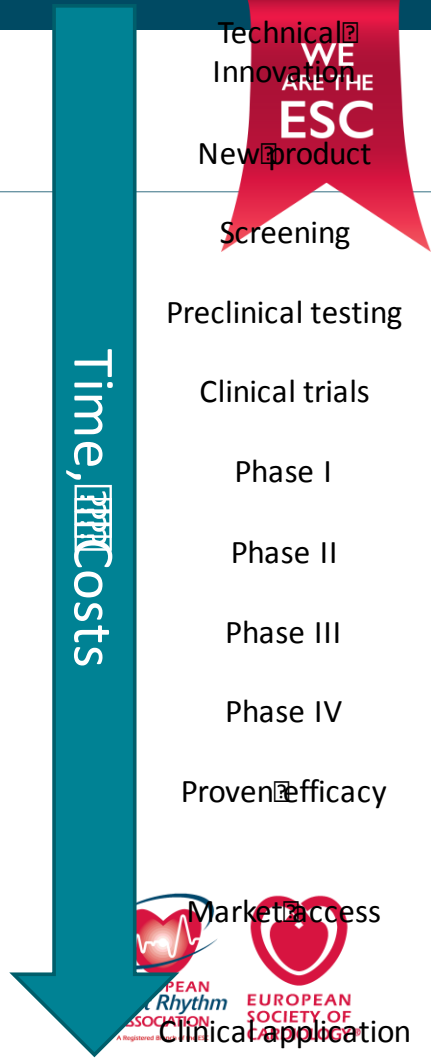
The problem: innovation, but at what price?

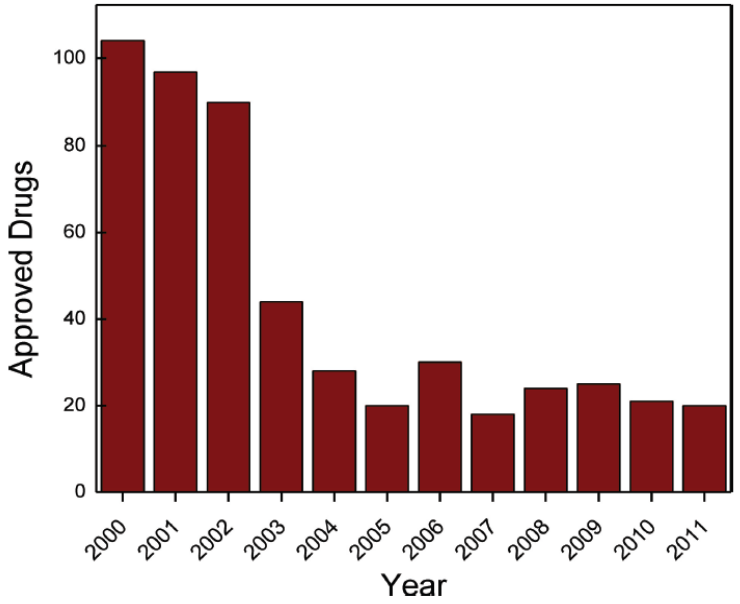
- **Cardiovascular health care needs new tools, drugs**
- **Time between development and market access, reimbursement becomes increasingly long, reducing return on investments of companies**
- **Conflicting interests of the various stakeholders:**
  - Patients
  - Industry
  - National, European economy
  - Insurance companies
  - Hospitals
  - …….

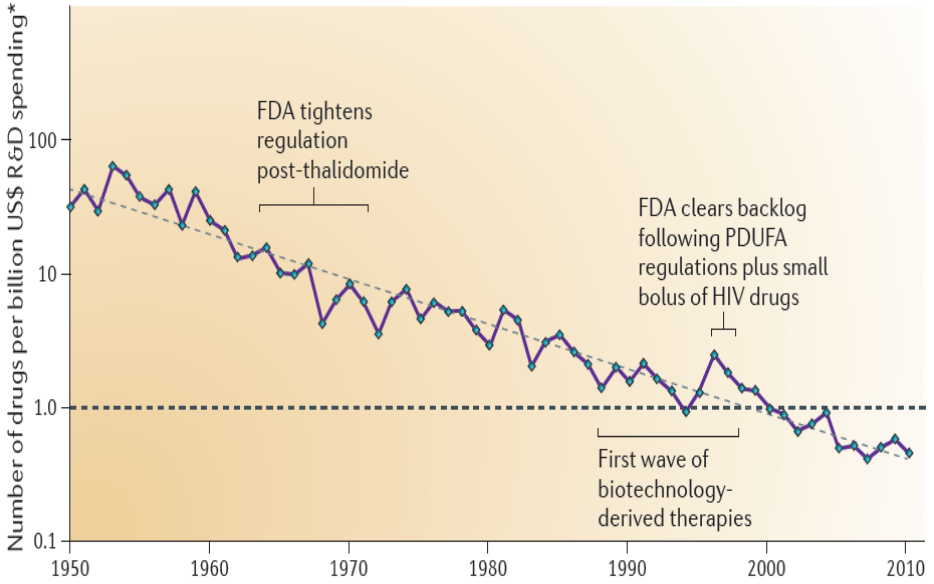


Examples of innovation in EP

- ECG and mapping tools
- Ablation catheters
- Leadless pacemakers
- subQ ICD
- NOACs

Approval of drugs is becoming increasingly more difficult and more expensive

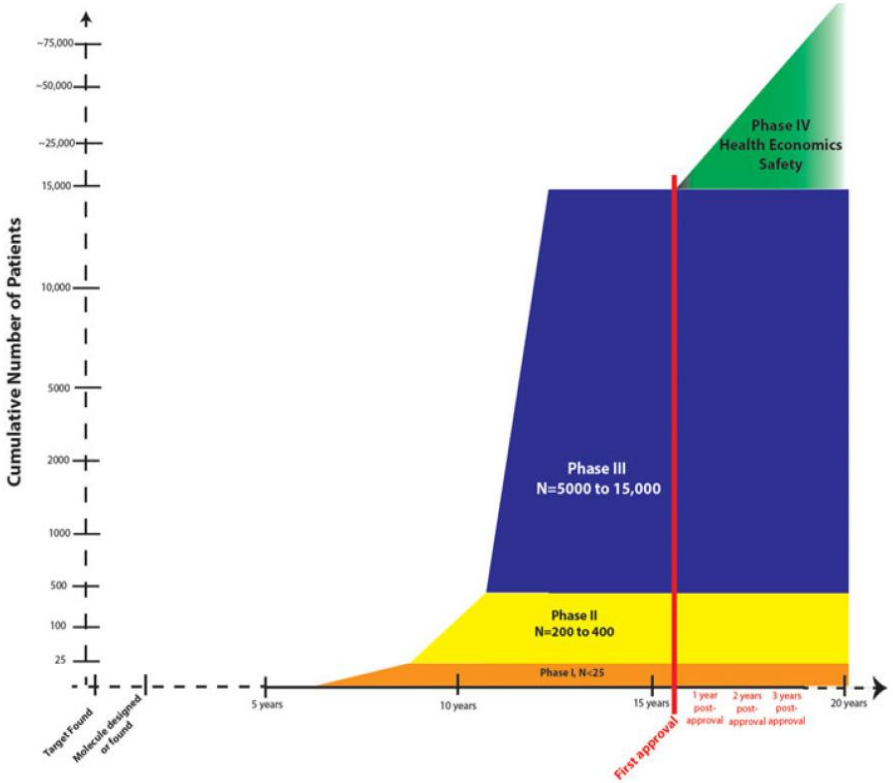




Loscalzo J. 2011 Lewis A Connor lecture. *Circulation.* 125:638-645 (2012)

Scannel et al. 2012
Nature Rev Drug Discov 11: 191-200

Traditional model for drug development



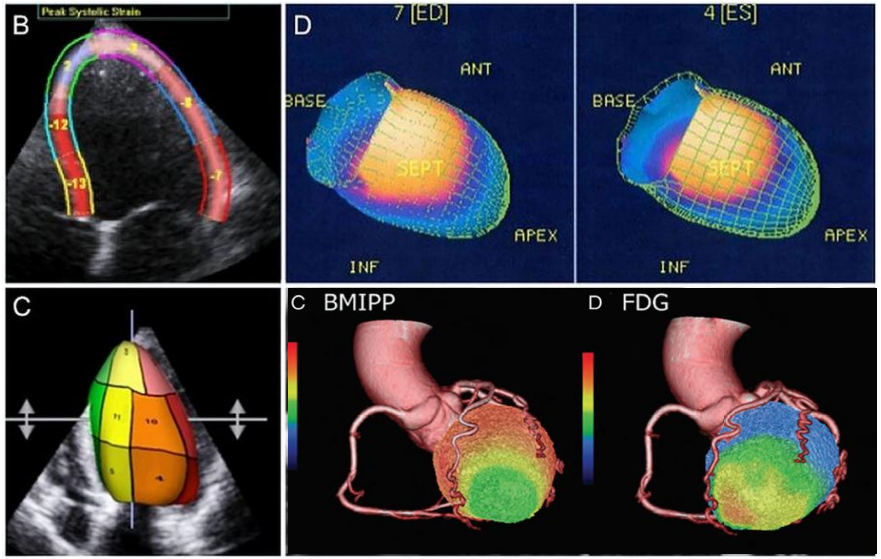
- Proven additional benefit of new therapy is increasingly difficult
- (Rare) event driven outcome
- Performed in poorly selected populations (mismatch of mechanism of disease and therapy) → low efficacy
- Costs for 1 drug 1.2 to 12 billion (if failures are included)

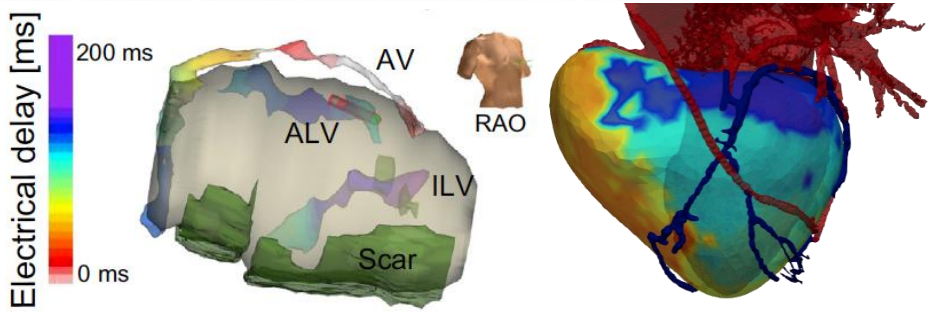
Jackson N, et al. *Eur Heart J.* (2015)

Possible solutions

- **Better identification of the disease of the patient**
  - Multimodal imaging
  - Genetics
  - Big Data
  - Computer models
- **Adjust therapy/study population to the geno/phenotype**
  - Personalized medicine; better defined study populations
- **More involvement of patients**

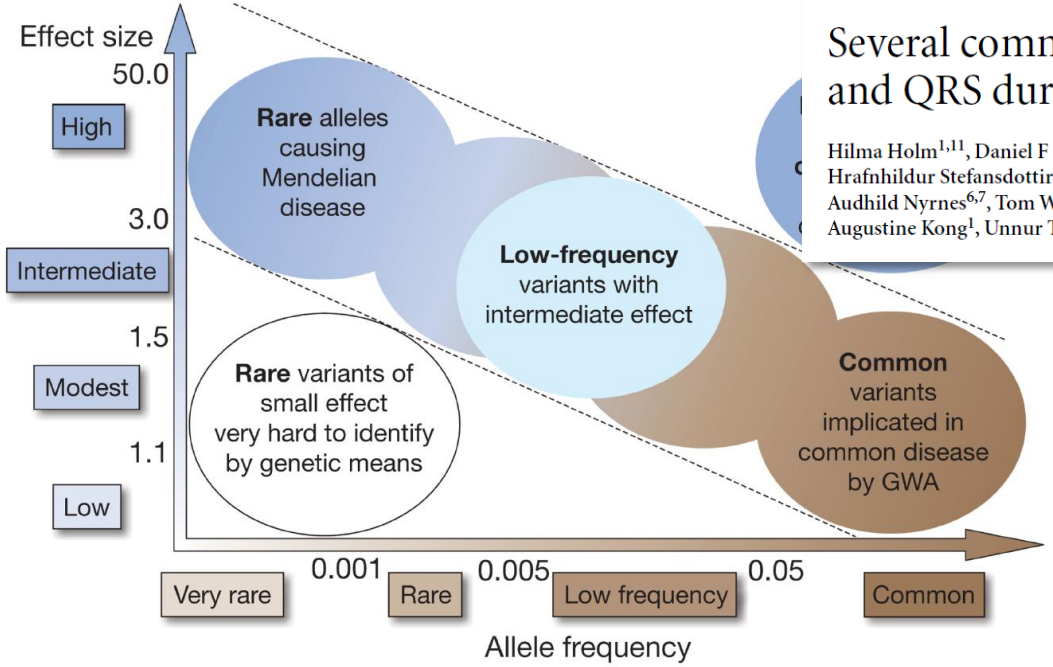
Multimodal imaging





- Echo: Strain (speckle tracking), Intraventricular flow patterns
- MRI: late enhancement, T1 mapping
- Electrical: contact/non-contact
- PET scan: metabolism, flow, catecholamines
- Molecular imaging emerging

New kid on the block: low-frequency ~ intermediate effect variants



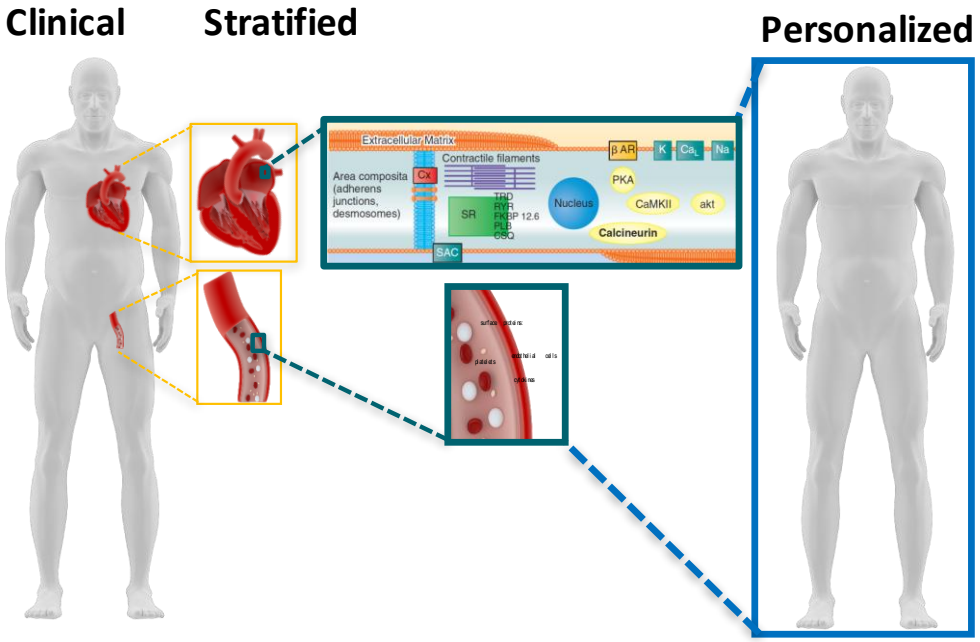
Manolio T, et al. *Nature* 2009; 461, 747-753

Several common variants modulate heart rate, PR interval and QRS duration

Hilma Holm[1,11], Daniel F Gudbjartsson[1,11], David O Arnar[2,3], Gudmar Thorleifsson[1], Gudmundur Thorgeirsson[2,3], Hrafnhildur Stefansdottir[2], Sigurjon A Gudjonsson[1], Aslaug Jonasdottir[1], Ellisiv B Mathiesen[4,5], Inger Njølstad[6], Audhild Nyrnes[6,7], Tom Wilsgaard[6], Erin M Hald[8], Kristian Hveem[9], Camilla Stoltenberg[10], Maja-Lisa Løchen[6,8], Augustine Kong[1], Unnur Thorsteinsdottir[1,3] & Kari Stefansson[1,3]

Locus	Gene	SNP	HR	PR	QRS
4q21	ARHGAP24	rs7660702		2.5·10-17	
6p21	CDKN1A	rs1321311			2.7·10-10
10q21	DKK1	rs1733724			6.5·10-8
3p22	SCN10A	rs6795970		9.5·10-59	3.5·10-9
12q24	TBX5	rs3825214		7.4·10-13	0.00011
7q23	CAV1	rs3807989		3.0·10-13	9.4·10-11
14q11	MYH6	rs365990	9.4·10-11	1.8·10-	

Personalized Cardiovascular Medicine for better definition of study patients

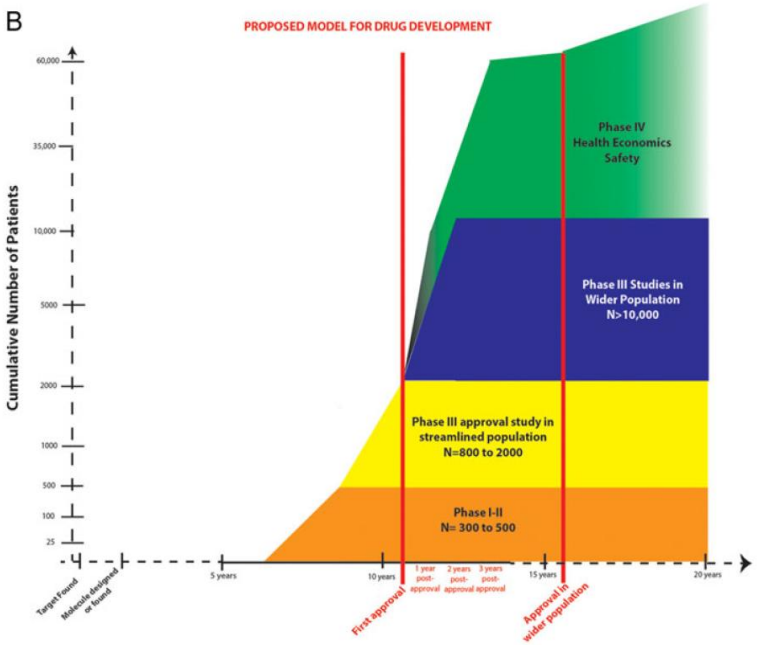


Clinical diseases and risk factors

Imaging of heart and vessels

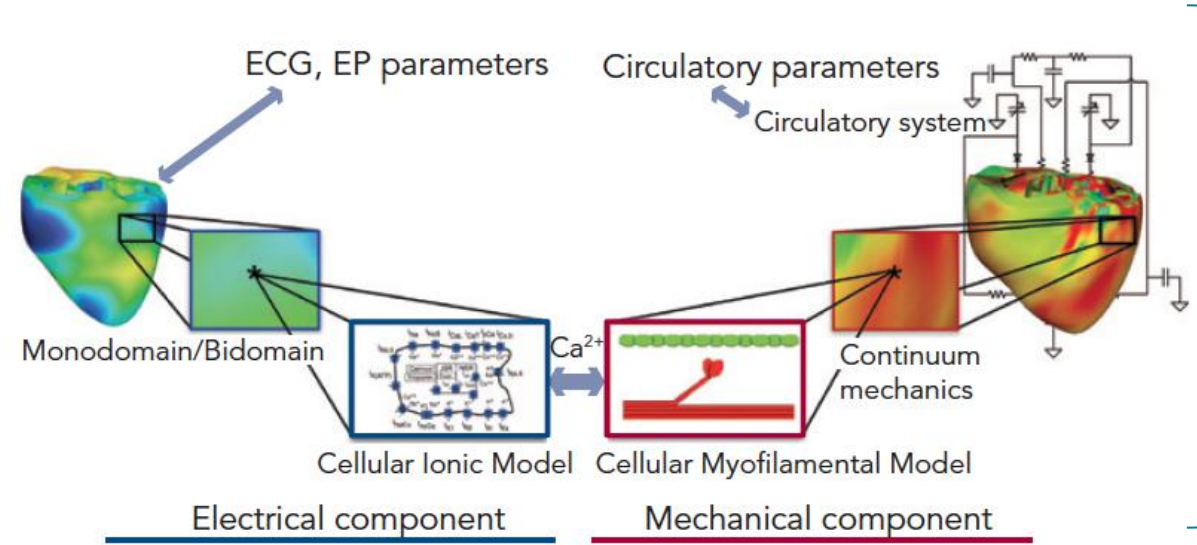
Molecular disease processes in heart tissue and blood (molecular imaging, biomarkers, genetics)

Integration into personalized disease management



ESC CRT position paper. Kirchhof P et al, *Eur Heart J*. 2014;35(46):3250-7.

Computer models → virtual clinical trials



Diagnostic measurements

Personalized model

Virtual clinical trial

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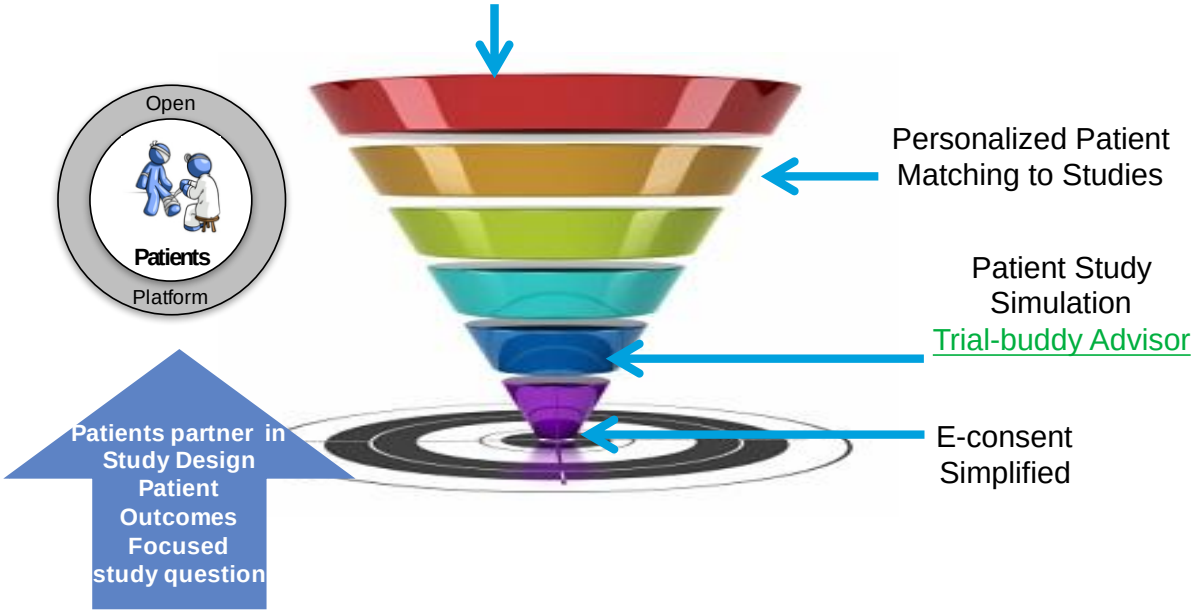
Big Data, machine learning for better patient selection and outcome measures

- **Only small percentage of clinical data is used for medical research**
- **More data to come:**
  - Implantable loop recorders, blood pressure sensors
  - Wearables, smart-phones, watches: CONTINUOUS, REAL LIFE data (no snap-shot outpatient measurement)
- **Apply the "Google, Facebook" approach to health care and research**

Please the (trial) patient

Information on trials and drug

https://mytrialbuddy.com: extensively informs patients considering participation in trials
http://meetforpatients.com
http://www.patientsacademy.eu/index.php/en: Patients' Academy on Therapeutic Innovation, EUPATI



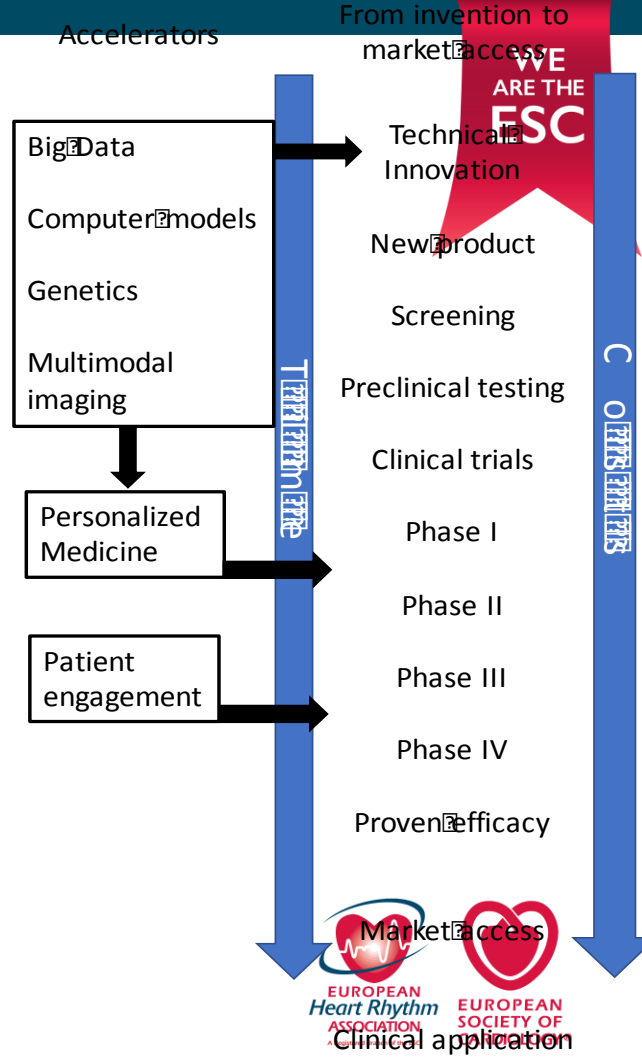
- Use technology in their interest

- Lay summary of the trial results
- Provide personal results/effects

Factors that can accelerate innovation

- New technologies can lead to technical innovation
- Smarter study designs
  - Based on mechanism of disease rather than clinical presentation
  - Reducing require number of patients, costs, time

EHRA: 2nd EHRA Innovation Forum to explore collaboration and funding of new initiatives



EHRA, ESC to address stakeholders

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- Regulatory affairs sometimes complicated
- Not well understood delays (up to 6 years!) between approval and reimbursement of new devices:
  - Budget considerations?
  - Administrative incompetence?
- Poor return on investments → decrease innovation???

- EHRA to be involved in admission of new therapies, communication with EU, insurance companies, hospital organizations
- EHRA stimulates national societies to monitor the process in their country

European Heart Journal (2016) **37**, 140–144
doi:10.1093/eurheartj/ehv275

CURRENT OPINION

Barriers to cardiovascular device innovation in Europe

Fausto Pinto[1]*, Alan G. Fraser[2], Josef Kautzner[3], Katja Kreutzer[4], Stéphane Piat[5], Markus Siebert[6], Panos Vardas[7], and Stephan Windecker[8], The Cardiovascular Round Table (CRT)†