Access to and affordability of medicines and diagnostics

EUPATI, AIDS Action Europe, EATG, MPE
Tamás Bereczky

STEP-UP: Skills Training to Empower Patients

Topic for this module

Medicines are too expensive, and so patients who need them don't have access to them.

Where and how can you / civil society intervene in the system and make a meaningful impact?

- The right to health is a fundamental human right
- Focus on evidence and strengths
- Think out of the box / creatively
- Be realistic

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Some starting thoughts

To gain a **general understanding** of the following:

- ✓ Drug development stages
- ✓ European drug licensing
- ✓ General themes in European drug pricing
- ✓ Different national systems of pricing and reimbursement
- ✓ The concept of health technology assessment
- ✓ Universal health care in HIV and co-morbidities
- ✓ Ideas on how to influence decision-making in practice across the processes of drug development and access

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Kate Morgan, Policy Manager, Myeloma Patients Europe, as presented at EHA2017

Drug development

- Lengthy, risky and difficult process
- Patient organisations focus on drug development to understand:
  - Pipeline of treatments
  - How trials are designed, patient and market centricity
  - How industry make decisions on drug development
  - Availability of clinical trials
  - Barriers to setting them up and how to overcome these
  - How medicines reach (or don't reach) patients

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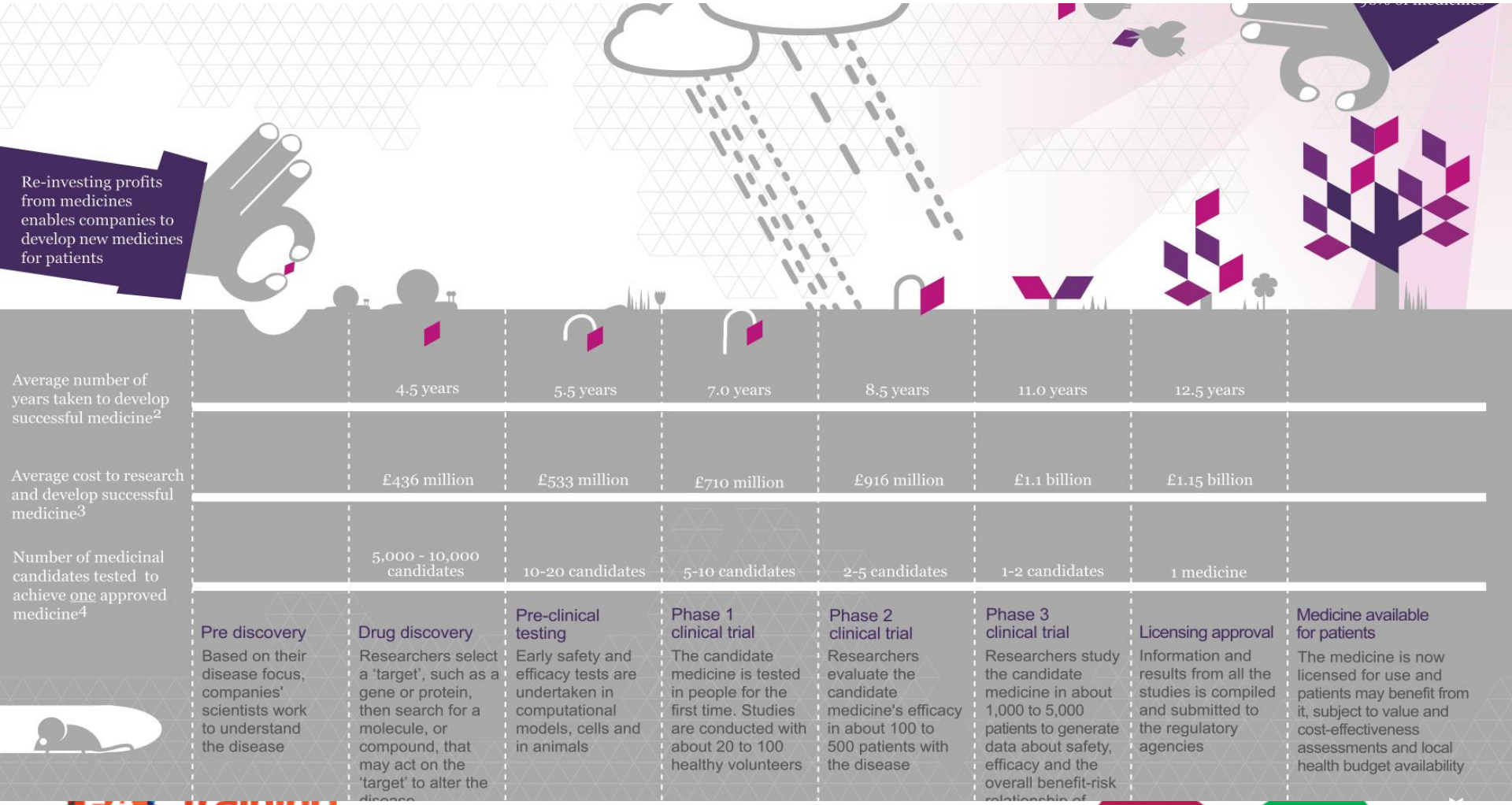
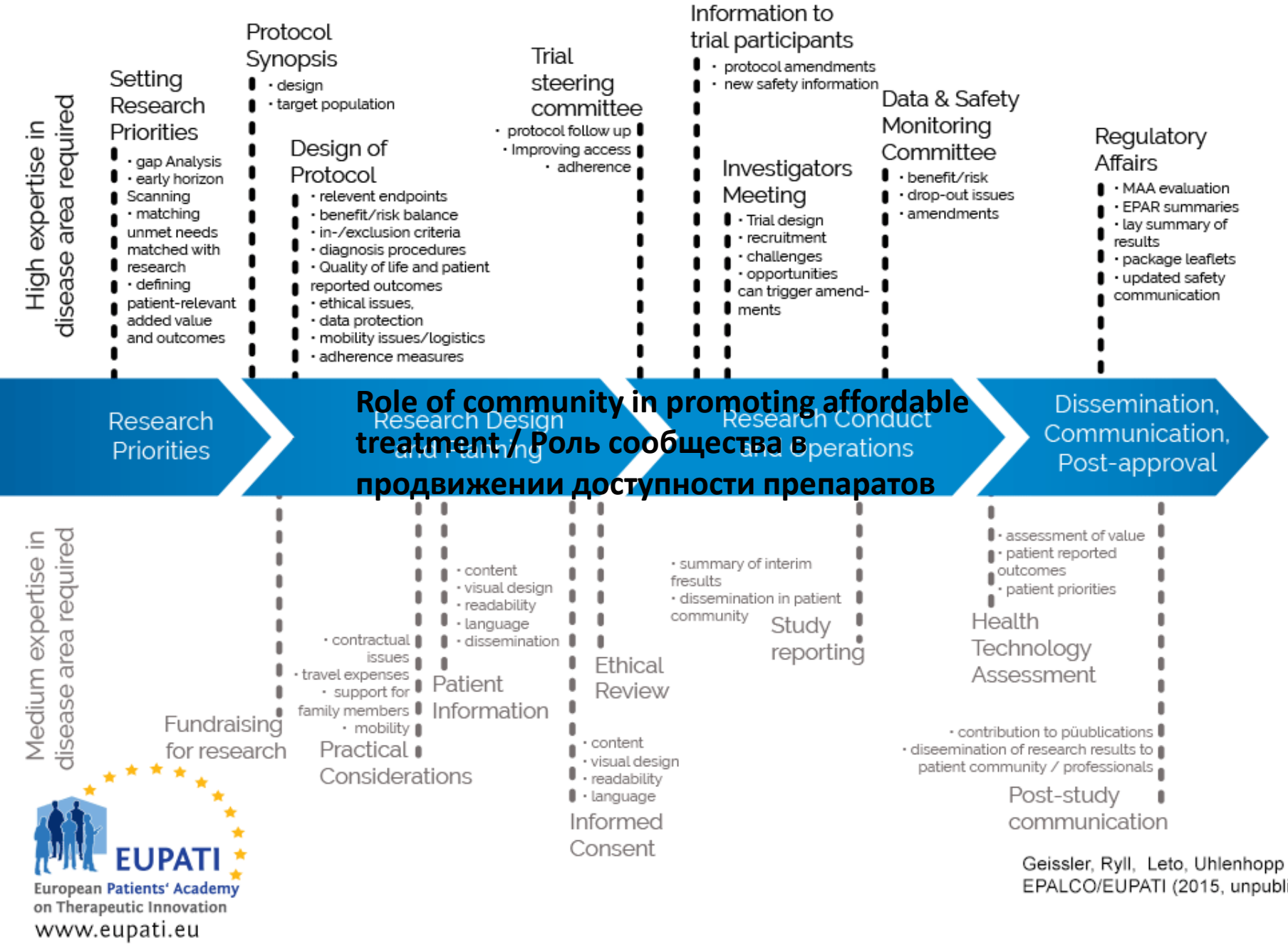
How are medicines developed?



Patient involvement in medicines R&D



EUPATI
European Patients' Academy on Therapeutic Innovation
www.eupati.eu

Geissler, Ryll, Leto, Uhlenhopp
EPALCO/EUPATI (2015, unpublished)

Trends in clinical trials

- Moving towards genetic and stratified medicine
- Trial populations are becoming smaller and drugs are being licensed on earlier phased data (e.g. daratumumab in myeloma and other cancers) – presenting issues for reimbursement
- New drugs and drug combinations are expensive – **affordability and value are becoming more important**

Kate Morgan, Policy Manager, Myeloma Patients Europe, as presented at EHA2017

Patents / intellectual property

- A legally provided and secured **monopoly** for the manufacturing of a certain product
- Granted by a state or an intergovernmental organisation that holds the authorisation to do so
- Valid usually for 20 years + special cases and extensions
- Seen as a necessary tool to protect the market and ensure steady revenue stream for more research
- Has become an extremely complex legal field/business
- Also seen as blocking access to public goods
- Several models of **challenging** patents within the legal system

Patents – points of interest

- **SPC** = Supplementary protection certificate (see Truvada®). They compensate for the long time needed to register a product
- Evergreening – Tricky extensions of patent protection to ensure increased revenue streams (e.g. Efexor – Efexor-XR – Pristiq)
- **Voluntary licensing** – The patent holder grants the manufacturing license as it wishes to another party, against royalties paid
- **Compulsory/mandatory licensing** – A government or an international organisation assumes the license/patent for a reason acknowledged in TRIPS – **DAAs and India**
  - Epidemiological emergency, public health reasons
  - No novelty
  - Economic crisis
- Activists can (and should) do **patent opposition**

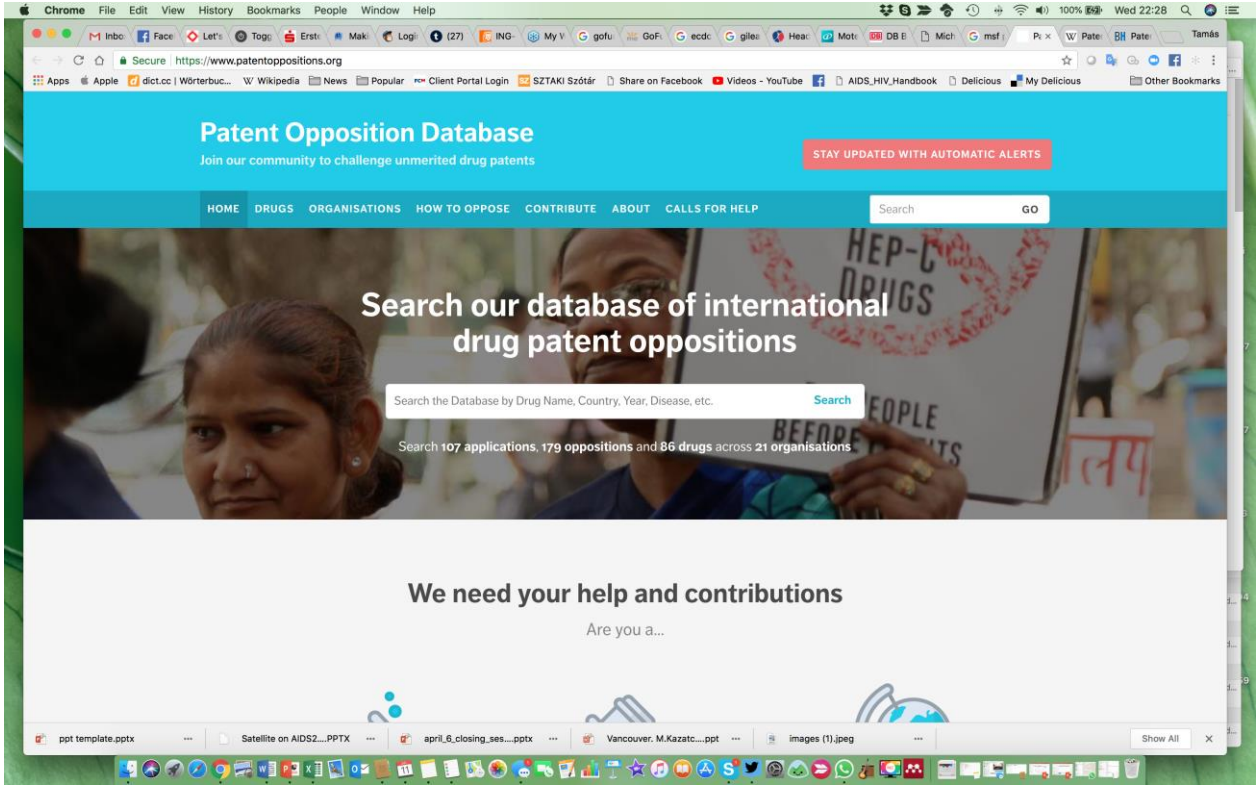
Free trade agreements

- Trans-Pacific Partnership
- Trans-Atlantic Trade and Investment Partnership
- EU Free Trade agreements with Moldova, Ukraine and Georgia all contain test data exclusivity which can delay generics' introductions
- Free flow of goods, reduced or no tariffs, simplified procedures
- Confidential conditions
- Prioritize the interests of multinational pharmaceutical and medical companies over patients worldwide and at home
- Severe limitations on generic medicines
- Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement of the World Trade Organisation (WTO) are overruled

TRIPS flexibilities

- Narrow the gaps in the way these rights are protected around the world, and to bring them under common international rules.
- Establishes minimum levels of protection that each government has to give to the intellectual property of fellow WTO members to strike a balance between the long-term benefits and possible short-term costs to society.
- Society benefits in the long term when intellectual property protection encourages creation and invention, especially when the period of protection expires and the creations and inventions enter the public domain.
- Governments are allowed to reduce any short-term costs through various exceptions, for example to tackle public health problems.
- The TRIPS Agreement allows governments the use of compulsory licensing for pharmaceuticals (and other patents) in certain well-defined cases.

Patent opposition



Consider cooperating and expanding your work in this area

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Introduction to drug licensing

- Different to national approval and reimbursement
- Determines whether a new drug, following Phase I-III clinical trials, is safe and effective
- No judgement made on the cost-effectiveness or whether health services should make it available although closer working between HTA and EMA/FDA

Kate Morgan, Policy Manager, Myeloma Patients Europe, as presented at EHA2017

Patient involvement in licensing

- Importance of patient involvement in decision-making
- CHMP committee involves patient representatives and they do provide industry with access to patients earlier in the process (through scientific advice)
- However, the earlier the better. Important for industry to have patients involved in the design of clinical trials
- “Patient preference” studies growing in importance

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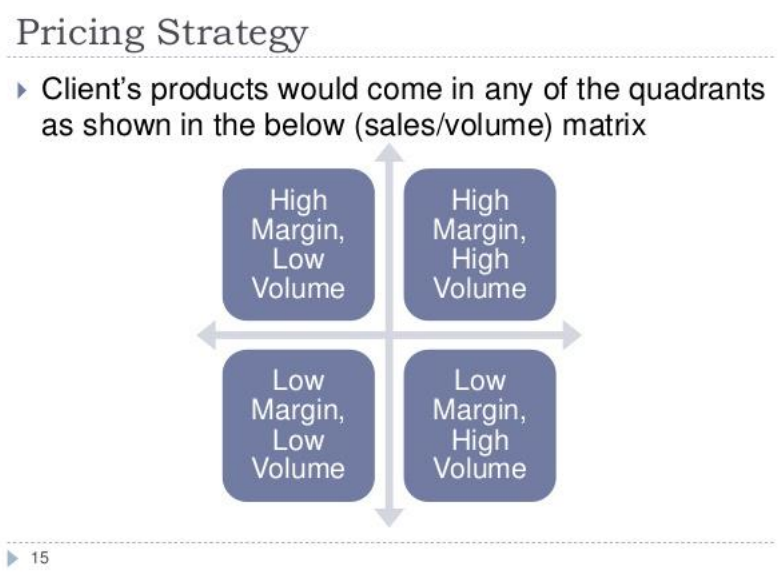
How are prices determined?

- Many different models
- Kept under secrecy
- Ultimately a business decision
- **We know very little**



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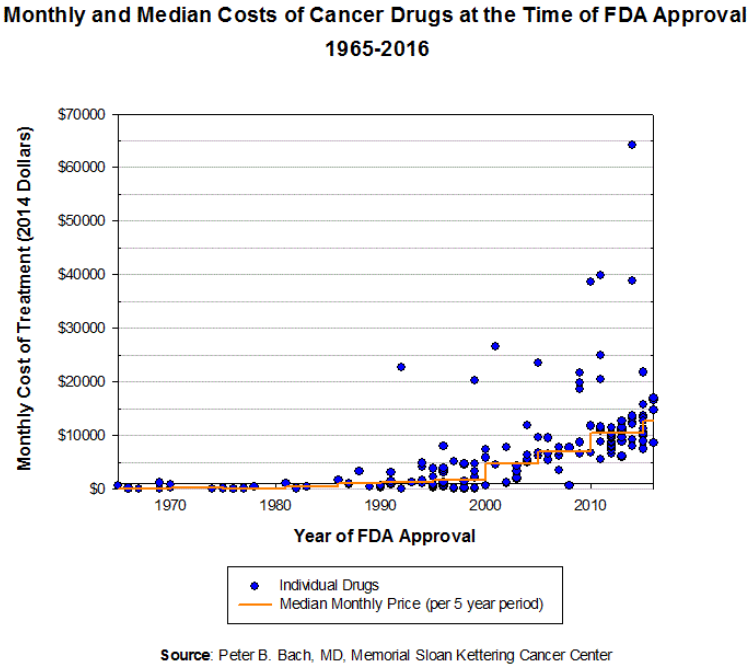
General points on drug pricing

- Prices for new medicines are set nationally
- However, there are global factors at play
- Confusingly, the “list price” is rarely the price paid for a new drug – there are ways of discounting it
- Drugs are priced individually, so in HIV or hepatitis, combination treatments can be very expensive at list price



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Eric Low, Independent Healthcare Consultant. Executive Chairman, Amyloidosis Research Consortium, as presented at EHA2017

How does drug pricing impact on patients?

- Across Europe, patients are routinely denied access to new treatments – price is one of the reasons
- Evidence suggests that drug pricing is not in line with societal views, value or on health systems willingness to pay
- Health systems are under pressure for price cutting, resulting in poor decision-making

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Global pressures on drug pricing

- Pharmaceutical pricing is a global process and is profit driven. US market is a key influence on drug pricing
- Reference pricing in the EU, means that companies want to secure higher prices in certain countries
- Pharmaceutical companies have internal pricing pressures (national vs EU vs global) – the ethos and portfolio of a company can determine pricing actions (e.g. Takeda and ixazomib)
- These all collectively influence the price of a new drug

Eric Low, Independent Healthcare Consultant. Executive Chairman, Amyloidosis Research Consortium, as presented at EHA2017

Thoughts on the system of drug pricing in Europe

- It is too complex and rigid
- Favours suppliers rather than payers
- Pricing to what markets will withstand – often excessive and indefensible
- Confusion between affordability and value and cost-cutting and efficiency
- Mediocrity has been rewarded (me-too drugs)
- Confusion about definition of innovation
- Increasingly problematic, particularly in publically funded health systems

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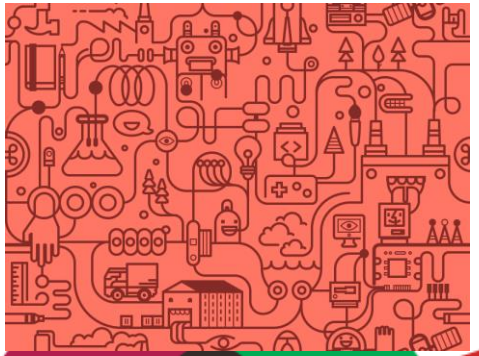
Potential solutions?

- Drug pricing needs to be more needs/demand-driven
- Better data is required / clinical trials transparency
- New pricing mechanisms
- Cost reduction – utilising capabilities of academic research infrastructure and networks
- Patients and patient groups can help align a system that is broken around patients
- Change required by everybody and at all levels

Eric Low, Independent Healthcare Consultant. Executive Chairman, Amyloidosis Research Consortium, as presented at EHA2017

How does drug pricing operate in your country?

- In Finland, the Pharmaceutical Pricing Board assesses the price of a drug which is submitted by the pharmaceutical company. This is linked to reimbursement, as they determine whether to reimburse the drug at the same time
- In Romania, Norway and Israel, they use the “reference pricing” model. This uses the price of drugs in a number of other European countries to determine a “ceiling” price a company can charge for a medicine
- In Germany, companies are free to price at launch. However, price is controlled through reimbursement policies



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Discounting and volume purchasing

- List price is rarely the price paid for by the health service
- Companies can discount their drug at different stages, however, this is usually confidential to protect their list “reference” price
- Locally, it is possible to purchase treatments on volume to reduce the price

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Reimbursement

- Reimbursement basically means that a new drug is paid for and provided by a national health service
- Decision-making on reimbursement can either be national (e.g. government, HTA body) or local (e.g. municipalities, hospitals, districts), depending on how a health system is set up
- Most decision-making on new medicines involves a cost-benefit analysis, in relation to how much money a country has to spend on healthcare
- Different models across Europe
- Do you pay anything in the pharmacy?
- What about ARVs?

Eric Low, Independent Healthcare Consultant. Executive Chairman, Amyloidosis Research Consortium, as presented at EHA2017

Reimbursement

- Some countries have specific “health technology assessment” (**HTA**) bodies which make decisions on new medicines
- HTA is a formal health economic process which looks at whether or not a drug is/how valuable to a health service – there are a range of different formula used to calculate the value (e.g. **QALY**)
- Other countries have bodies conduct a less formal assessment of a new drug, however, still looking at the cost-benefit of a new medicine
- Different ways of engaging patients

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Issues with reimbursement

- Complex and difficult to navigate
- New drugs are increasingly expensive and the pathway is crowded
- European drugs budgets are limited and access challenges are developing – how can healthcare systems pay for new medicines?
- Arguably, what patients value is becoming more important
- Increasing pressure on company prices to justify the value of new medicines
- In cancers, we are currently fixing problems of the past – need to anticipate the future

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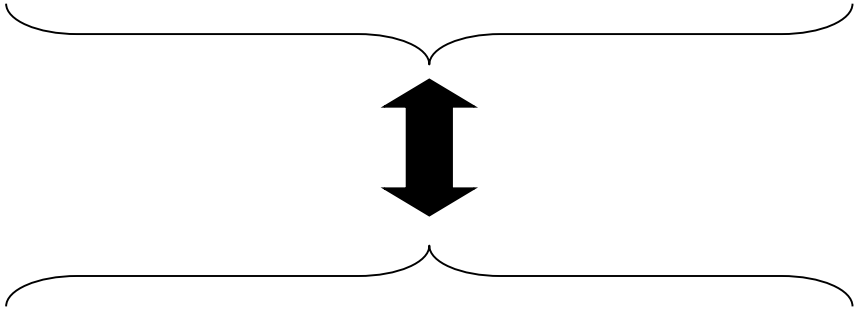
Universal Health Coverage and Access

- Universal health coverage is the goal that all people obtain the health services they need **without risking financial hardship** from unaffordable out-of-pocket payments
- **Universal health coverage** is attained when people actually obtain the health services they need and benefit from financial risk protection.
- **Access**, on the other hand, is the opportunity or ability to do both of these things. Hence, universal health coverage is not possible without universal access, but the two are not the same.

Universal health coverage and access 2

- *Health supply terms*
  - Availability
  - Affordability
- *Health demand terms*
  - Utilisation
  - Acceptability



Access =

how much a population can **reach** health services

Coverage =

the share of a population **eligible** (beneficiaries) for a set of interventions

Universal access in the context of HIV/AIDS treatment, prevention and care interventions

1. **Universal access for treatment** is treatment that is reachable, affordable and acceptable to all those in need

2. **Universal access for prevention** is along the same lines as for treatment: key prevention services should be reachable, affordable and acceptable to all those who need it: "all districts should have VCT, PMTCT, condoms, sex & AIDS education (general public, schools)", target population programs, which could be specified and could be measured

3. **A core package** of HIV/AIDS treatment, prevention and care interventions is defined, each one occurring in one of the four **loci**: hospital, health centre, community, home

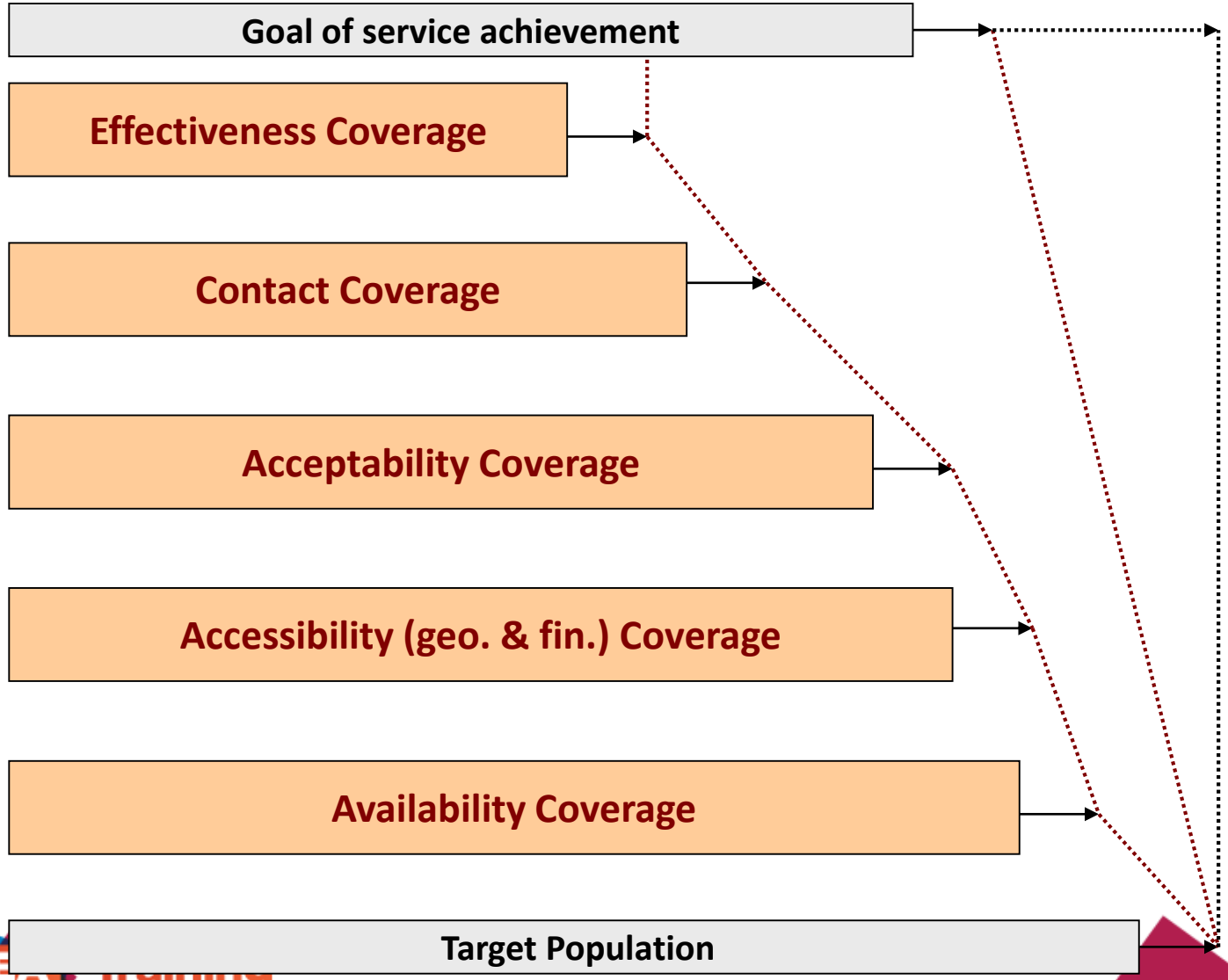
4. The framework for universal access is **target driven**

Tanahashi – the WHO's 5 criteria

Access has three dimensions:

- **Physical accessibility.** The availability of good health services within reasonable reach of those who need them and of opening hours, appointment systems and other aspects of service organization and delivery that allow people to obtain the services when they need them.
- **Financial affordability.** Measure of people's ability to pay for services without financial hardship. It takes into account not only the price of the health services but also indirect and opportunity costs. Affordability is influenced by the wider health financing system and by household income.
- **Acceptability.** People's willingness to seek services. Acceptability is low when patients perceive services to be ineffective or when social and cultural factors discourage them from seeking services.

Tanahashi: Health Service Coverage Diagram



Source: Tanahashi T. Bulletin of the World Health Organization, 1978, 56 (2)

Summary

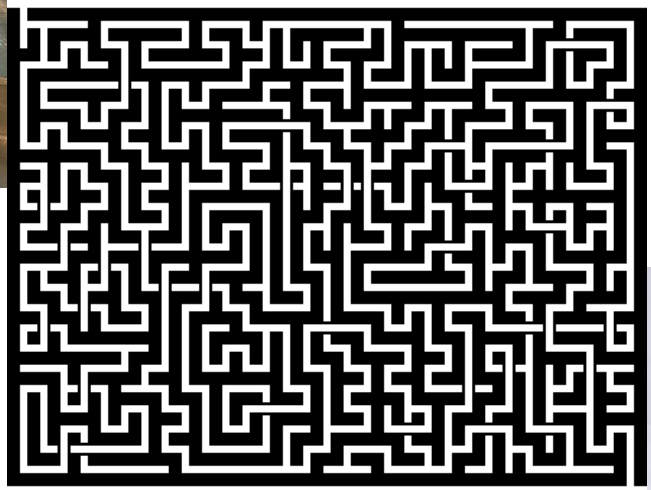
- Pricing is a national process but there are significant international influences
- High prices affect patients
- Pricing is linked to reimbursement. Change is needed in the pricing system to ensure that national access is sustainable, with better use of existing legal tools
- Patients and patient groups can play a role in delivering solutions to pricing and reimbursement by being a honest broker

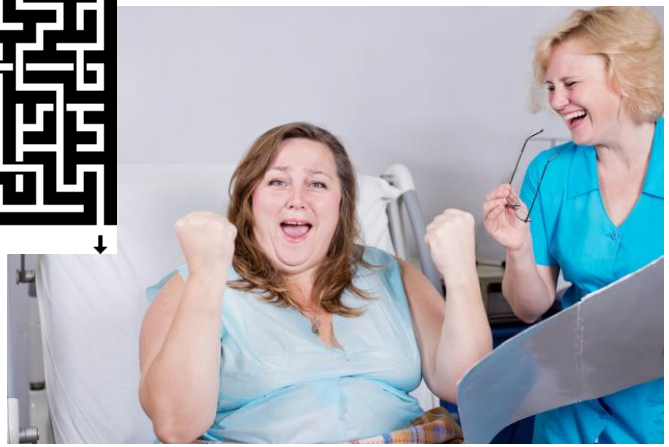
Eric Low, Independent Healthcare Consultant. Executive Chairman, Amyloidosis Research Consortium, as presented at EHA2017

Practical exercises / discussion on access and affordability

EUPATI, AIDS Action Europe, EATG, MPE
Tamás Bereczky

Avenues of access





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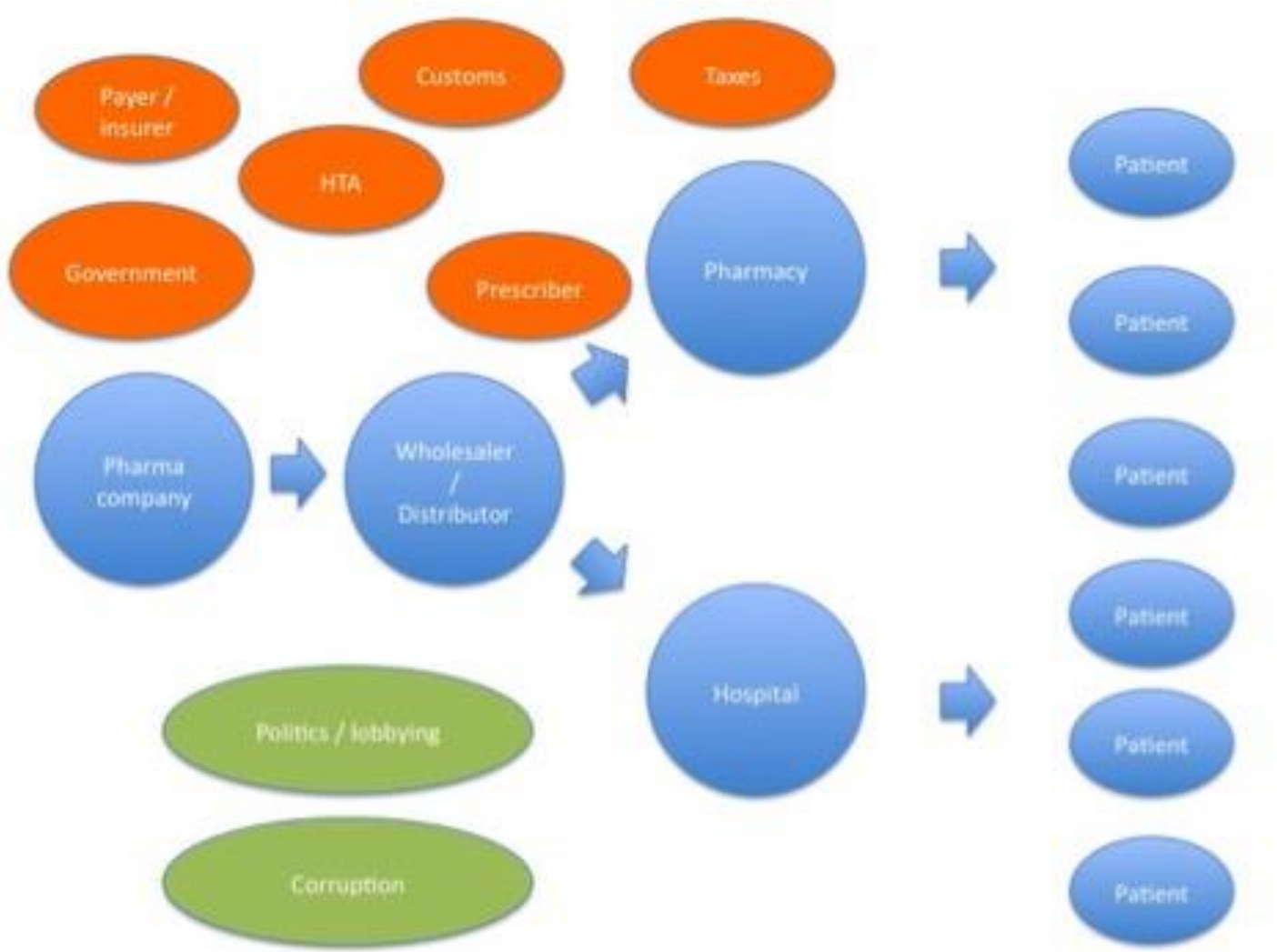
How do medicines get to the market?



Discussion exercise

- What do you think the role of patient organisations should be in drug development, pricing and reimbursement processes
- What do you think patient organisations can do to influence the availability of clinical trials in their respective country?
- What do you think patient organisations can do to influence and prepare for national approval of new medicines?
- How can we prepare for future medicines access challenges?
- What can the EATG and other organisations do to help patients on drug development and access issues?

What are your key issues?

- Research and development of medicines
- Pricing of medicines
- Generics
- IP
- Monitor the national regulatory processes
- How are medicine prices set in Europe?
- Negotiating and advocacy skills
- More knowledge for better advocacy

Building arguments

- More evidence
- Industry perspective
- Regulators' perspective
- Academia/science perspective
- Patients' view
- Collecting evidence
- Devising a strategy
- Channeling anger and outrage
- Actions

Reflect on this!

- Where do you see any points of intervention?
- What can these points of intervention be?
- Who can be our allies and adversaries, who are neutral?
- What tools or skills do you need?
- How do you get along in this maze?

- Framing the current debate on the Sustainable Development Goals (SDGs)
  - a paradigm shift: health system development rather than developing vertical programs by exception
- Current debates in R&D models promoting:
  - status quo
  - reform of the system: de-linkage of R&D and price and international treaty

- Fact: the R&D model that the world currently has produced innovative life-saving medicines

BUT

- There was innovation in medicinal product before the current monopoly system based on patent protection was strengthened with the TRIPS agreements
- There are serious problems with access to optimal treatment options and a very concerning way of prioritizing research, e.g. the lack of investments in innovative research for TB shows a failure of the model to deliver needed life-saving medicines

Regional challenges

- We acknowledged that the main barrier in EECA is probably not only the price, but the political will.

BUT

- the experience of sub-Saharan African countries shows that high price is also a disincentive to put into place programmes.

EATG standpoint

In summary, EATG –

- sees potential in a European movement that addresses short, medium and long term goals of system change
- has decided to engage with the European Alliance for Affordable Medicines and Responsible R&D should become more vocal on access to affordable medicines in general and in pointing out the flaws of the current R&D model, e.g. we can at least demand an on-going high-level discussion at the UN and EU level. We can support initiatives that would address some of the flaws of the current system.
- We should become health systems advocates and contribute to achieving health systems that are better financed and resourced, and more effective.

UN High-Level Panel on Innovation and Access to Medicines

- UN Secretary-General High-Level Panel appointed by Ban Ki-moon in November 2015
- *Focus:*

  promoting **innovation** and **access to health technologies**

- *Objective:*

  to review and assess proposals and recommend solutions for **remedying the policy incoherence between** the justifiable **rights of inventors**, **international human rights law**, **trade rules** and **public health** in the context of health technologies

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UN High-Level Panel on Innovation and Access to Medicines

Recommendations

- IP laws and access to health technologies
- New incentives for research and development of health technologies
- Governance, accountability and transparency

European level processes

- The Council of the European Union – Conclusions from 17 June 2016
- Workshop: EU Options for Improving Access to Medicines – EP event on 14 July
- European Parliament Working Group on innovation, access to medicines and poverty-related diseases – Statement
- EC HTA proposal
- EU SPC, pediatrics and orphan drugs incentive review
- Copenhagen Economics Report "Study on the economic impact of the Supplementary Protection Certificate and pharmaceutical incentives and rewards in Europe", commissioned by the European Union

European level processes

The Council of the European Union – Conclusions from 17 June 2016

- The Council invites member states to increase collaboration and data sharing
- Explore possible strategies on voluntary joint price negotiations in coalitions of Member States, that have expressed interest to do so;
- Exchange HTA-methodologies and assessment outcomes through EUnetHTA and the HTA Network as already foreseen under the Joint Action EUnetHTA
- Recent EC proposal for HTA collaboration - see EPHA position and analysis

What are your local challenges?

- Privatisation of some health care services
- How are ARVs and DAAs financed?
- Risks?
- Stock-outs
- Corruption
- Stigma & discrimination

A twisted system?

- Intellectual property regulations
- Patents
- Evergreening
- TRIPS
- Parallel import
- Mandatory licensing
- Voluntary licensing
- Clinical trials

Alternative models for better access and R&D

- Why do we need them?
- Stakeholders
- Points of intervention in the system
  - What?
  - Where?
  - How?

- Direct negotiations on country level Parallel, semi-legal routes of access
- EU Joint Procurement Procedure
- Medicines Patent Pool
- Service de-linking
- Affordable Medicines Initiative
- DND*i* model

Direct negotiations

- Portugal, Scotland, France etc. in HCV
  - Lack of transparency
  - Competition across countries
  - Growing inequalities
  - Relatively quick access for patients in need

What are the **upsides** and **downsides**?

Parallel, semi-legal routes of access

- Buyers clubs
- Travelling abroad
- Corruption and irregular practices
- Clinical trials
- Buying on the internet

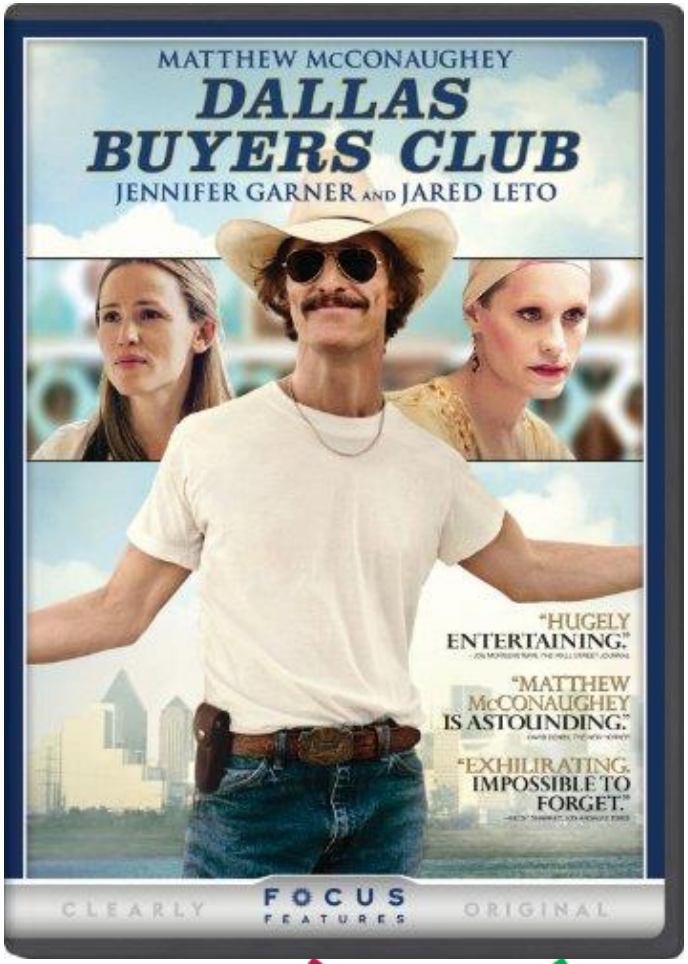
What are the **upsides** and **downsides**?

Social pharmacies

- Example from Greece
- What other examples do you know?

Buyers' club

- Just like in the old days!
- Prescription for the generic names of the active ingredients according to genotype
  - Harvoni = sofosbuvir + ledipasvir
  - Daclinza + Sovaldi = daclatasvir + sofosbuvir
- TreatAsia
- London Buyers' Club
- Moscow, St.Petersburg



Joint Procurement Procedure

- Originally devised for vaccines
- Process started in 2008
- Joint Procurement Agreement signed and entered into force in 2014
- Somewhat controversial, slow progress

The Medicines Patent Pool

- United Nations-backed public health organisation working to increase access to HIV, viral hepatitis C and tuberculosis treatments in low- and middle-income countries.
- Partners with governments, industry, civil society, international organisations, patient groups and other stakeholders to forecast, prioritise and license needed medicines.
- Encourages generic manufacture and the development of new formulations through patent pooling.
- Agreements with 7 patent holders for 12 HIV antiretrovirals and for 1 hepatitis C direct-acting antiviral. Generic partners have distributed 7.2 million patient-years of WHO-recommended HIV medicines to 117 countries.

Delinking Revenues from Sales

- Chatham House proposal
- Tackling the problem from the industry side
- Finding an alternative model to reward companies for R&D
- Eliminating or redesigning the model of intellectual property

What are the **upsides** and **downsides**?

European Alliance for Responsible R&D and Affordable Medicines

- **Secure affordable prices now.** Address urgent access and affordability issues for life-saving medicines by negotiating lower medicine prices and using effective price control mechanisms, including compulsory licences.
- **Put an end to pharmaceutical monopolies.** Promote generic and biosimilar competition.
- **Implement full transparency of pharmaceutical R&D, as well as medicine price setting.**
- **Promote a new biomedical R&D model** (delinkage of pricing from R&D, incentives that are need-driven etc.)

The DND*i* model

- Drugs for Neglected Diseases *Initiative*
- Model of virtual biotech company
  - Identification and screening of libraries
  - Medicinal chemistry
  - Pharmacology and pharmacodynamics
  - Formulation development
  - Manufacturing
  - Conduct of clinical trials
- Product Development Partnership (PDP)

The DNDi model 2

- Originates from rare tropical diseases with high unmet need – of no interest for companies
- Need of safe, affordable, easy-to-use and efficacious treatments for neglected patients
- Robust R&D portfolio that covers the entire drug discovery process
- Capacity building (economic development) by strengthening existing capacities in disease-endemic countries
- Pragmatic strategy towards drug discovery that has evolved from a hunter-gatherer approach

The DNDi model 3

- Discovery and the “S” Rule
  - Sourcing
  - Screening
  - Selection of Series
- Data mining/low-hanging-fruit approach: aim is to identify compounds well characterized for development
- Development of innovative new drugs through long-term lead optimization programs
- Researchers are funded as fee-for-service contractors and make no claim to any intellectual property
- The PDP for drug development relies on strong partnerships between industry and academia, and on sharing of knowledge that is often held as proprietary by different partners

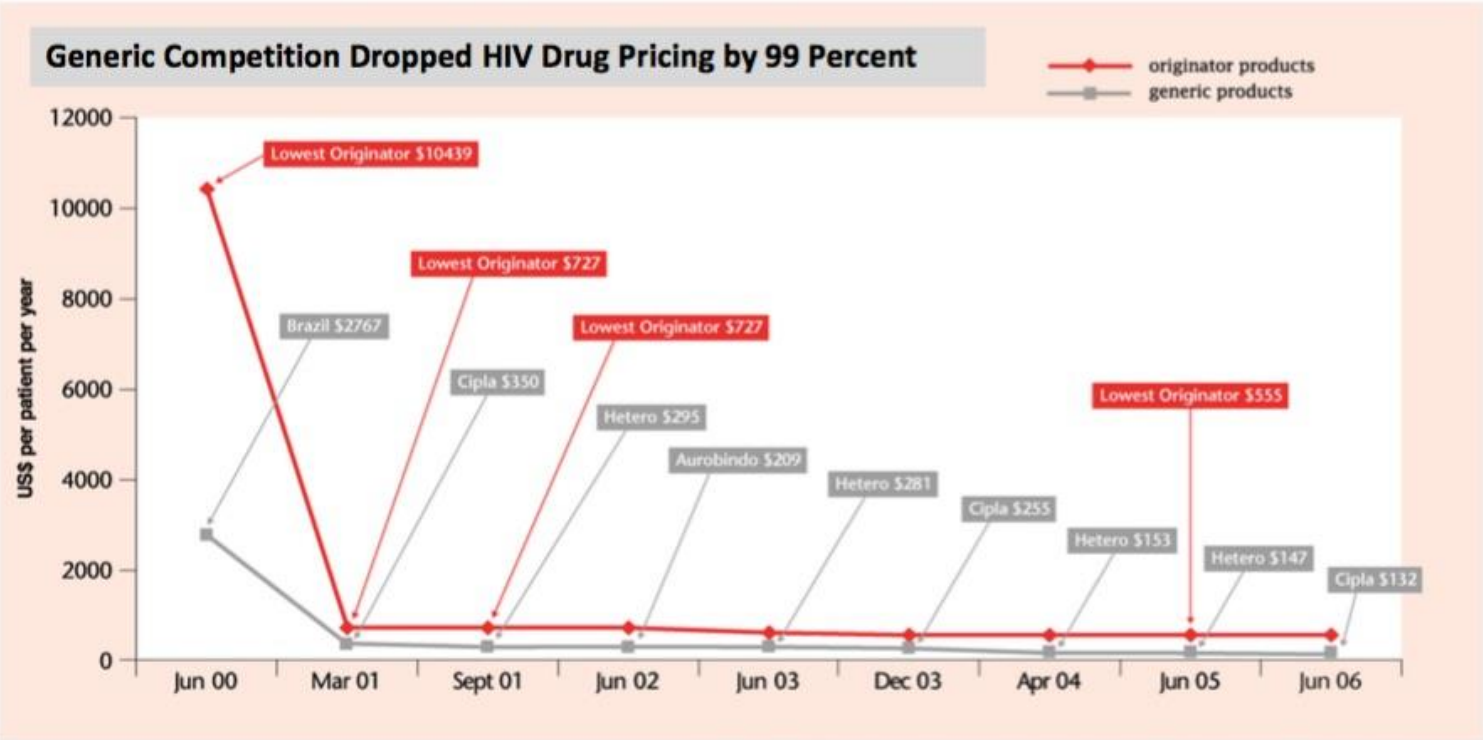
The role of generics

ACCESS CAMPAIGN

MEDECINS SANS FRONTIERES

Competition = The Price of AIDS Drugs Fell by 99%

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES



Source: MSF Untangling the Web of Antiretroviral Price Reductions, 15th Edition, July 2012

The role of generics 2

- How generics saved Africa from an even bigger AIDS disaster
- Example from Hungary (TDF and LVD)
- Problems in EU
- Quality issues
- Information issues
- How can you contest original manufacturers?

Case studies from the HCV field

- Sofosbuvir
- Daclatasvir – Andrew Hill's analysis
- There are opportunities, but also risks
- Setting priorities
- Selecting a line of action and advocacy tools
- Doctors of the World – patent opposition

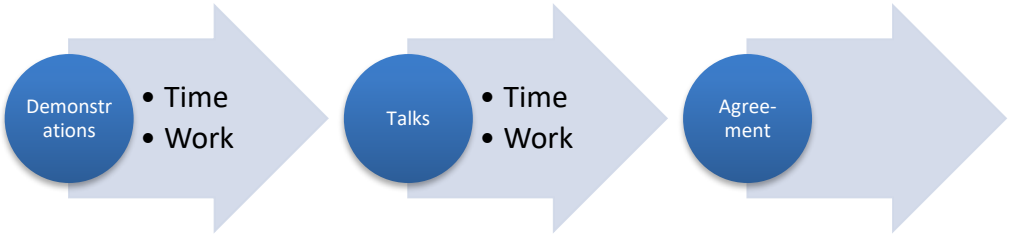
Street action of patients «The Condemned»

- **3,5** millions people have HCV
- **No** HCV State program
- **No** state funds
- **No** National Treatment Guidelines
- More than **€ 8 000** price for PEG-Inf per 48 weeks in retail
- **NO Access to HCV Treatment**

www.patients.org.ua
office@patients.org.ua

Patients of Ukraine asked Prime-Minister to procure medicines

SOF and other HCV medicines



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Additional resources

- http://www.eatg.org/publications/access-to-highly-effective-hepatitis-c-treatment-in-portugal-a-community-perspective/
- https://medicineslawandpolicy.org/useful-resources/
- EATG patient advocacy training manual in English and Russian: http://www.eatg.org/publications/treatment-advocacy-training-manual-english-and-russian-versions/
- AIDS Action Europe Pricing and Affordability training manual: http://www.aidsactioneurope.org/en/publication/affordability-medicines-and-diagnostics?position=2&list=mH47OQSs5HtHBBP_vE5uiLnrRMCEKx6C7gYLvaLJVWU
- The Impatient Patient: http://socio.hu/uploads/files/english/bereczky.pdf

Acknowledgements

- AIDS Action Europe
- EATG
- LeukaNET
- HEM-CAB
- Myeloma Patients Europe
- Ann Isabelle von Lingen
- Andrej Senih

THANK YOU

AIDS Action Europe

Tamás Bereczky

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