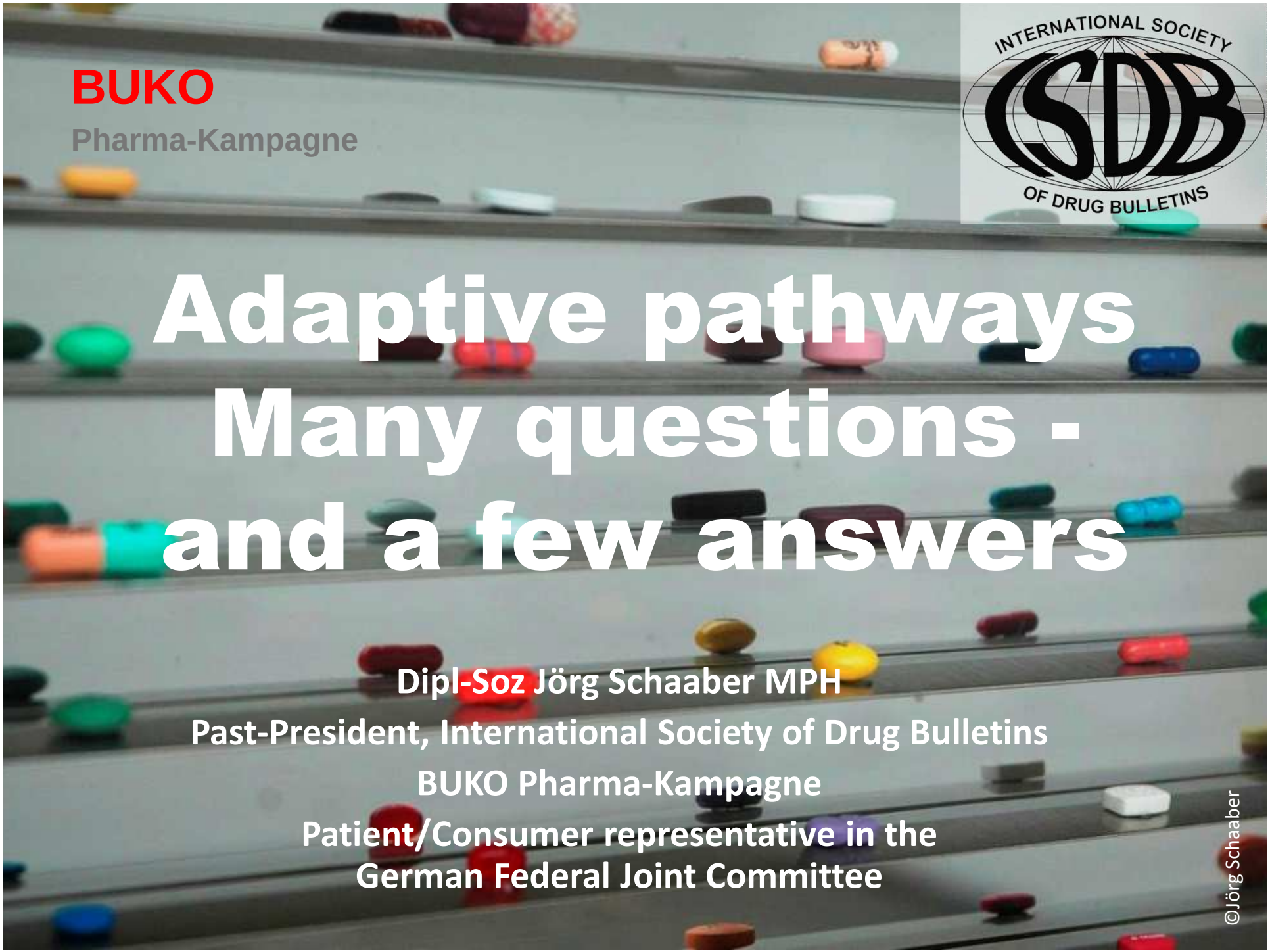
BUKO
Pharma-Kampagne
INTERNATIONAL SOCIETY
ISDB
OF DRUG BULLETINS
Adaptive pathways
Many questions -
and a few answers
Dipl-Soz Jörg Schaaber MPH
Past-President, International Society of Drug Bulletins
BUKO Pharma-Kampagne
Patient/Consumer representative in the
German Federal Joint Committee
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Taking about science?

… or power and money?

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Money
Earlier revenue stream & less trials

What is common among the examples is an attempt to strike a compromise between timely access for at least some patients and development of sufficient evidence for reliable benefit–risk assessment across a much broader population. The potential benefits for companies would be an earlier revenue stream than under a conventional licensing pathway and less expensive and shorter clinical trials.

Eichler et al. (2012) Clinical pharmacology & Therapeutics; 91, p 426

Is industry in need?

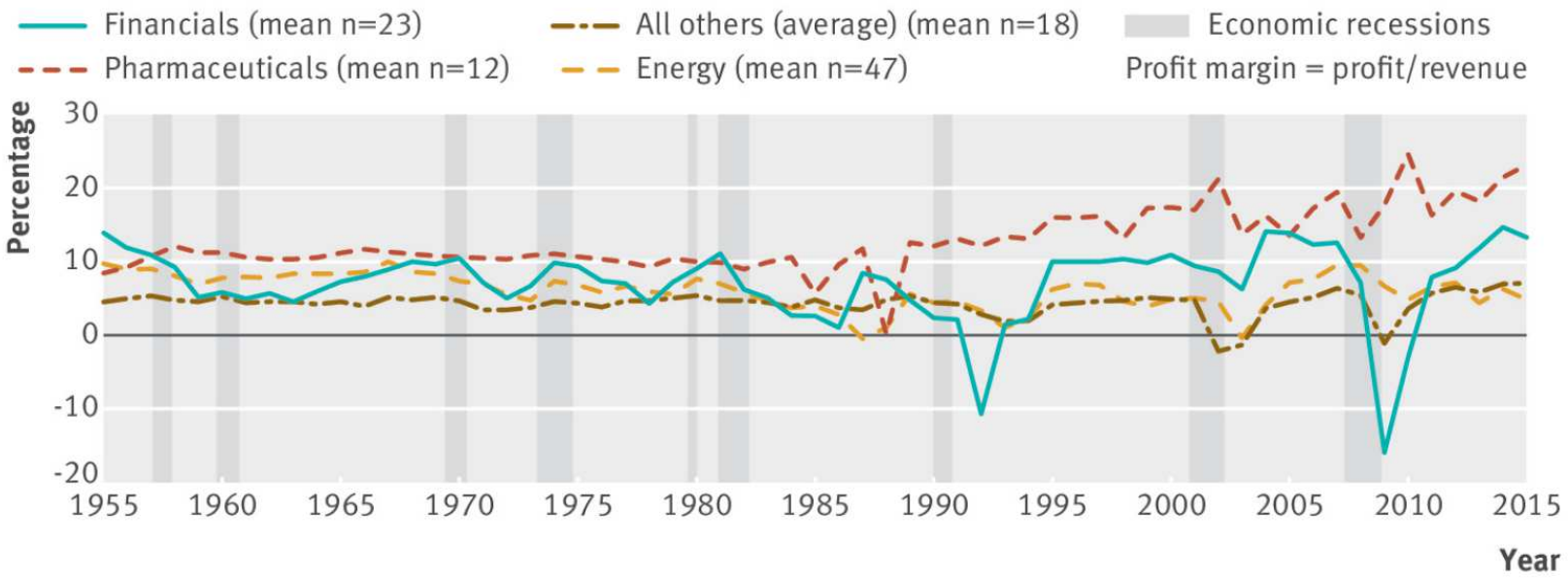


Fig 1 Fortune 500 average profit margin by sector over time

Roy V and King L (2016) BMJ; 354, p i3718

More revenue – more research?

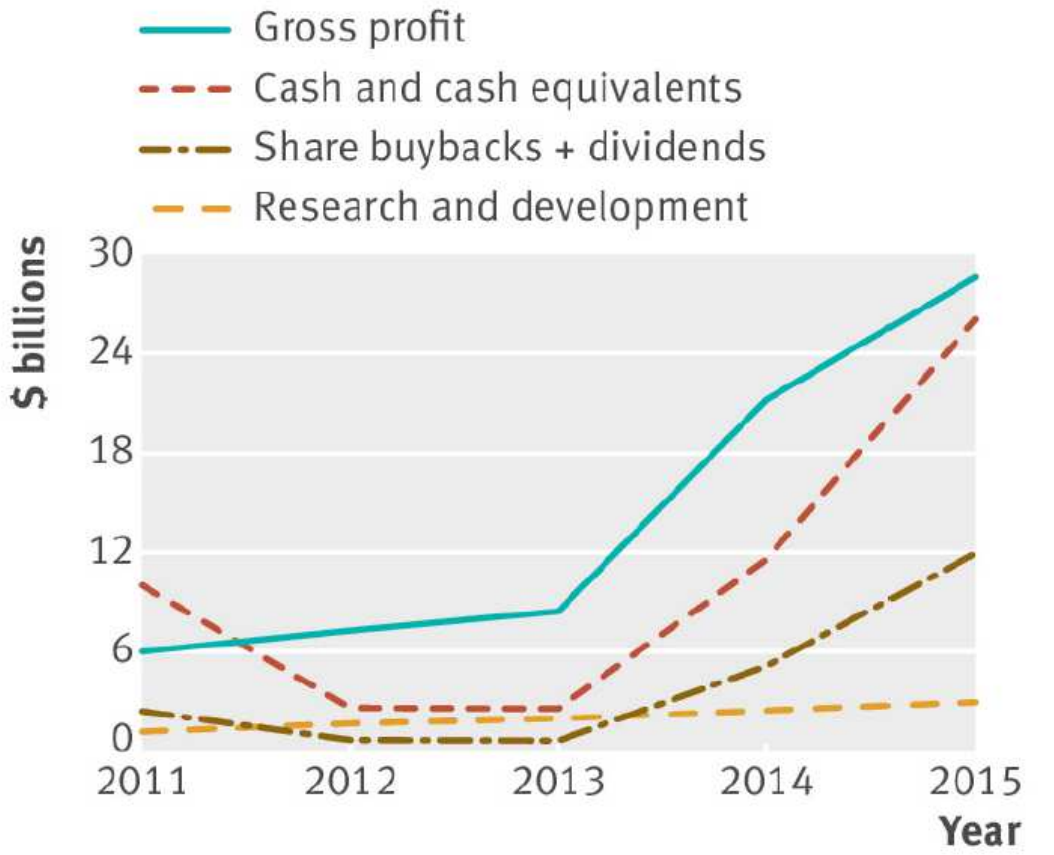


Fig 2 Gilead's key financial indicators ($bn)

Roy V and King L (2016) BMJ; 354, p i3718

AL/AP: Where comes it from?

- MIT industry sponsored think-tank NEWDIGS (New drug development paradigms)
- Bringing industry together with regulators and academia
- 2011 Participation of Hans-Georg Eichler (EMA) as Robert E. Wilhelm Fellow

http://betterscience betterhealth.com/hans-georg-eichler/ [accessed 18.3.2016]

Shaping change behind closed doors

Wouldn't it be great if, in NEWDIGS, we could strategically design and pilot new policies - and actually inform change?"

NEWDIGS participant with experience as a clinician, regulator, patient, & industry executive
April 2010

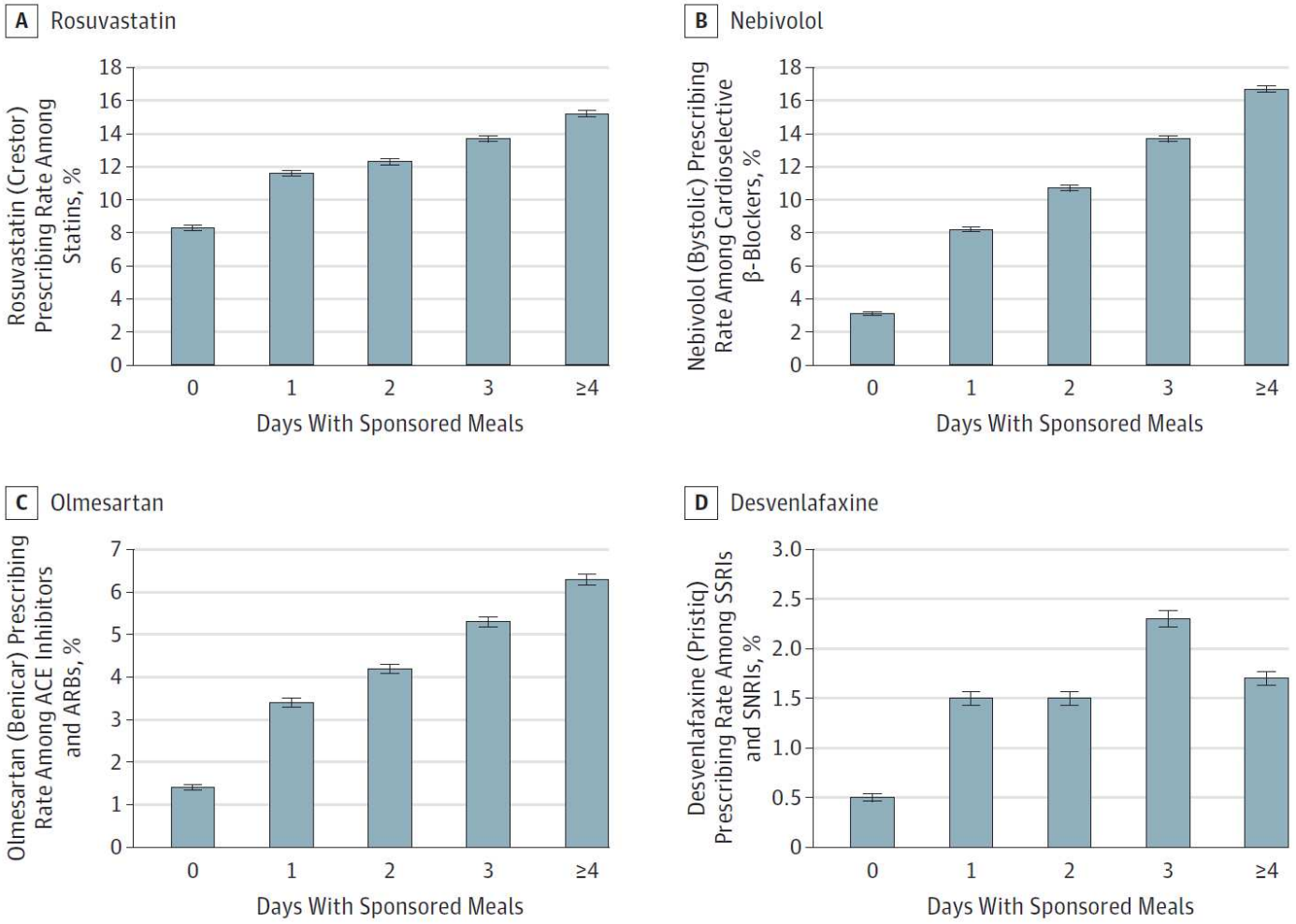
http://casmi.org.uk/wp-content/uploads/2012/11/GHirsch-Adaptive-Licensing-UK-Workshop-2April2012.pdf

Conflicts of interest do matter

- How much should those to be regulated (industry) influence how they are regulated?
- Should EMA (and HTA) become a co-developer of drugs?
- Risk of institutional capture

Sponsored meals and prescriptions

Figure 1. Target Branded Drugs as a Percentage of All Filled Prescriptions in the Class in 2013, Across Days Receiving Target Drug–Sponsored Meals



De Jong et al.(2016) JAMA Intern Med. doi:10.1001/jamainternmed.2016.2765

The role of patients

- Serve as justification (fast access)
- Which patients are consulted?
- Lending questionable decisions legitimacy
- Patients exposed to harm

Faster access for patients

Key argument AP and TTIP

STATE OF THE ART

Eichler et al (2015) Clinical Pharmacology & Therapeutics; 97, p 234

Table 1 Drivers and enablers of adaptive licensing (adaptive pathways)

Drivers
Patient expectations: demand for timely access and emphasis on unmet medical need
Emerging science: fragmentation of treatment populations and early disease interception
Healthcare systems under pressure: rise of payer influence
Pharma/investors under pressure: sustainability of drug development

PhRMA (2013) Request for Comments Concerning the Proposed Transatlantic Trade and Investment Partnership, 78 Fed. Reg. 19566, 10 May

The innovative biopharmaceutical industry strongly supports efforts to address regulatory differences and duplicative requirements that can impede efficiency in global drug development, review and evaluation. Addressing these important issues can help to enhance efficiency of drug development and optimize deployment of limited regulatory agency resources, and at the same time, lead to expedited patient access to new, innovative and life-saving medicines. With this in

What is a cure worth?

The safest drug that no one can afford or that arrives too late is of no benefit to a patient.

Mark W. Skinner, JD

Gene therapy for hemophilia – future scenarios for cost, capacity, and impact on therapy

The 9th WFH Global Forum on Research and Treatment Products for Bleeding Disorders

Montreal, Canada

23 October 2015

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FEDERACIÓN MUNDIAL DE HEMOFILIA

President/CEO of Institute for Policy Advancement

DISCLOSURES FOR: MARK SKINNER

Conflict	Disclosure - if conflict of interest exists
Research Support	Baxalta, Bayer, Biogen, Novo Nordisk, SOBI
Director, Officer, Employee	WFH USA, BloodSource, ATHN
Shareholder	n/a
Honoraria	Grifols
Advisory Committee	PCORI Rare Disease, NHF MASAC, Blue Cross Blue Shield MAP, Bayer HAAB, Novo Nordisk Fitness Camp
Consultant	NHF

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Patients: Lending legitimacy

Explicit and reproducible input from patients should facilitate the decision of regulators and payers to allow drug access at a given level of uncertainty, by lending legitimacy and public acceptance of the decision.

Eichler et al. (2015) Clinical Pharmacology & Therapeutics; 97, p 234

More harm?

Higher level of uncertainty

A key feature of AL […] is a stronger emphasis on communicating the higher than usual level of uncertainty to patients and providers

Eichler et al. (2012) Clinical Pharmacology & Therapeutics; 91, p 426

As the total number of trial patients diminishes because efficacy is shown earlier, the knowledge base about safety is smaller at the time of initial market authorization and coverage

Eichler et al. (2015) Clinical Pharmacology & Therapeutics; 97, p 234

Conflicting messages on AP

- Only for diseases were there is an unmet medical need (definition of need?)
- Also for other drugs?
- A better model for drug licensing in general?
- Just a process to make better use of existing marketing authorisation regulation?

AL as common pathway?

There are considerable challenges and benefits to fully implementing AL as the common pathway for drug approval. Overall, there seems to be sufficient merit in the current ideas to allow pilots to go forward to try to generate the data to determine whether AL offers a more favorable alternative to the current licensing paradigm

Eichler et al. (2012) Clinical Pharmacology & Therapeutics; 91, p 426

AL (not necessarily) for high unmet medical need?

Under AL, the development program is restructured to allow for early approval and coverage of a new compound for a limited population, typically (but not necessarily) with a high unmet medical need, based often on smaller initial clinical studies.

Eichler et al. (2015) Clinical Pharmacology & Therapeutics; 97, p 234

AP only for unmet medical need?

The adaptive pathways concept is not meant to be applicable to all medicines, but only to medicines that are likely to offer help for a patient population with an unmet medical need, and where the criteria for adaptive pathways apply.

EMA (2016) Final report on the adaptive pathways pilot. 28 July

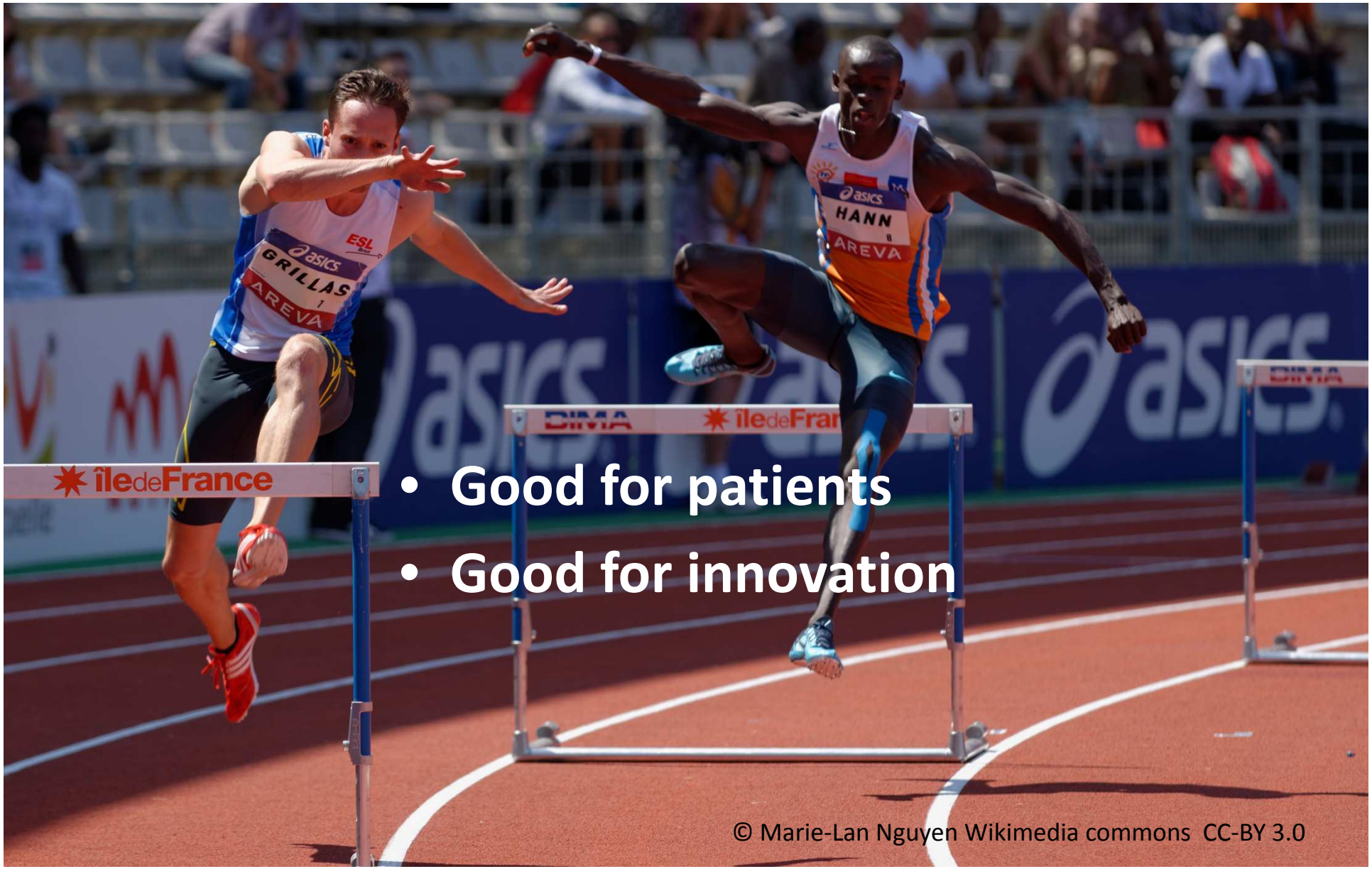
Conclusion: what is AL/AP about?

- Faster market access with less evidence
- Small phase II studies enough
- Surrogate outcomes instead of hard endpoints
- For limited patient groups (who can control?)
- Lower standards for evidence generation after marketing authorisation

What do we need?

- Better designed RCTs fully published
  - Patient populations that reflect morbidity patterns in society (age, health status, co-morbidities)
  - Meaningful endpoints (morbidity, OS, QoL)
  - Longer studies
- Comparison against therapeutic standard
- Better surveillance of ADRs
- Therapeutic advance as market entry criterion

Therapeutic advance paradigm



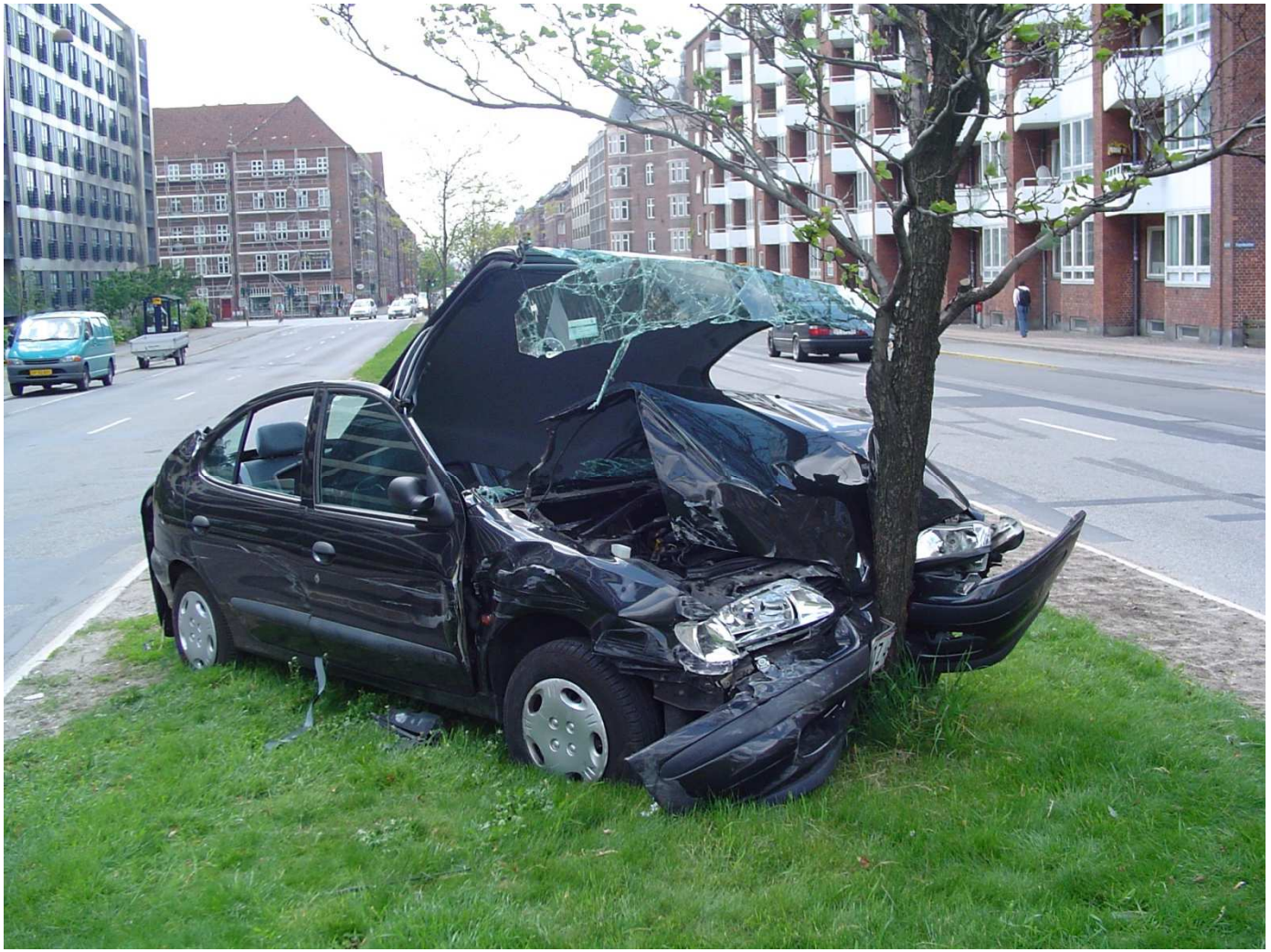
- **Good for patients**
- **Good for innovation**

US version of AP:
21th Century Cures Act

But it's important to recognize that this legislation [21th Century Cures Act], if not carefully crafted, could pose significant risks for FDA and American patients.
It is vital that the legislation accomplishes the twin goals of promoting innovation and preserving the safety and effectiveness standard. Innovative therapies are not helpful to patients if they don't work, or worse, cause harm. We must be able to strike the right balance between fast access and good science.

Califf RM (2016) Speech by Commissioner Robert M. Califf to the 2016 FDLI Annual Meeting www.fda.gov/NewsEvents/Speeches/ucm499475.htm

… faster is not always better



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