Be Greater Than

Development, Registration & Market Access of Orphan Drugs in EU

Matthew Webb, Pfizer Oncology Lead Czech Republic

Pfizer Innovative Health

Pfizer Oncology

What are *Orphan Drugs?*

Pfizer Oncology

EMA Definition: A medicine for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that is rare **(affecting not more than five in 10,000 people in the European Union)** or where the medicine is unlikely to generate sufficient profit to justify research and development costs.

Patient impact of rare diseases in EU

Be Greater Than

European Medicines Agency (EMA) Orphan drugs and rare diseases at a glance. 2016

Pfizer Innovative Health

Pfizer Oncology

Development & Registration

Be Greater Than

Generating necessary clinical data in rare diseases is difficult….

Pfizer Oncology

Low patient numbers make conducting clinical trials challenging

National & regional collaborations is key

Be Greater Than

…and low economic returns for Orphan Drugs could hinder investment in research

Pfizer Oncology

- Cost of developing new medicines relatively fixed, regardless of number of patients it will be used to treat
- Average costs of developing a new drug = $1.4bn
- Including earnings investors forego during 10+ years development takes bring cost to $2.6bn

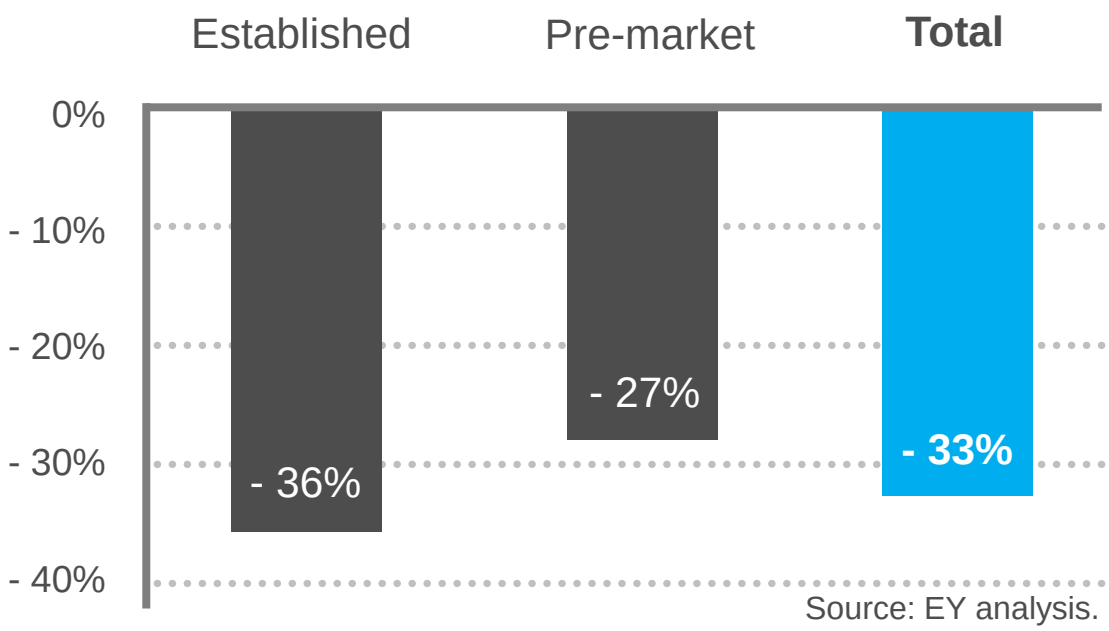
Be Greater Than

DiMasi, JA et al, 2016. Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics*, 47, 20-33.

Incentivising investment into rare diseases drug research in the EU

Evidence suggests incentives are working – data from USA

Figure ES-1: Estimated decline in investment in orphan drugs by type of developer under potential ODTC repeal



Source: EY analysis.

Impact of the orphan drug tax credit on treatments for rare diseases. EY, June 2015. Prepared for the Biotecnology Industry Organisation & the National Organisation for Rare Disorders

Pfizer Innovative Health

Pfizer Oncology

Market Access

Be Greater Than

We can categorise major EU HTA methodologies into two distinct categories

HTA systems that combine clinical and economic outcomes (e.g. cost/QALY)	HTA systems that primarily evaluate the clinical value >> pricing negotiation
NICE/SMC (UK)	IQWiG (Ger)
TLV/SBU (Swe)	HAS (Fra)
PBAC (Aus)	AIFA (Ita)
CADTH (Can)	
AOTMiT (Pol)	

Some markets have specific cost-effectiveness thresholds (e.g. UK, Pol, SK)

HTA systems that combine clinical and economic outcomes (e.g. cost/QALY)

Pfizer Oncology

Quality Adjusted Life Year

The number of years of life left for a group of patients following a treatment, adjusted for the quality of life during those years

EXAMPLE

Drug X provides a median OS 2 years great than comparator in a clinical trial

Due to side effects & disease symptoms, quality of life on scale of 0-1 is calculated as 0.5

QALYs gained = 1

Problems with Quality-Adjusted Life Years (QALYs)

Pfizer Oncology

Cost-effectivness analysis using QALYs suffers many limitations as a tool to improve patient-centered health care

1. INCOMPLETE: **Not designed to capture many important sources of value** to patients, the health care system, and the wider economy
2. UNRELIABLE: Heavily dependent on the measurement instrument being used, which produces **inconsistent and unreliable results**
3. THEORETICAL: Intended as a **theoretical tool for academic researchers**, not for desicions that impact actual patient lives
4. NOT PATIENT-CENTERED: Developed from population averages, which **ignore the health care needs and preferences of individual patients**
5. DISCRIMINATORY: Widely acknowledged by experts to **discriminate against people with disabilities** or **pre-existing conditions**

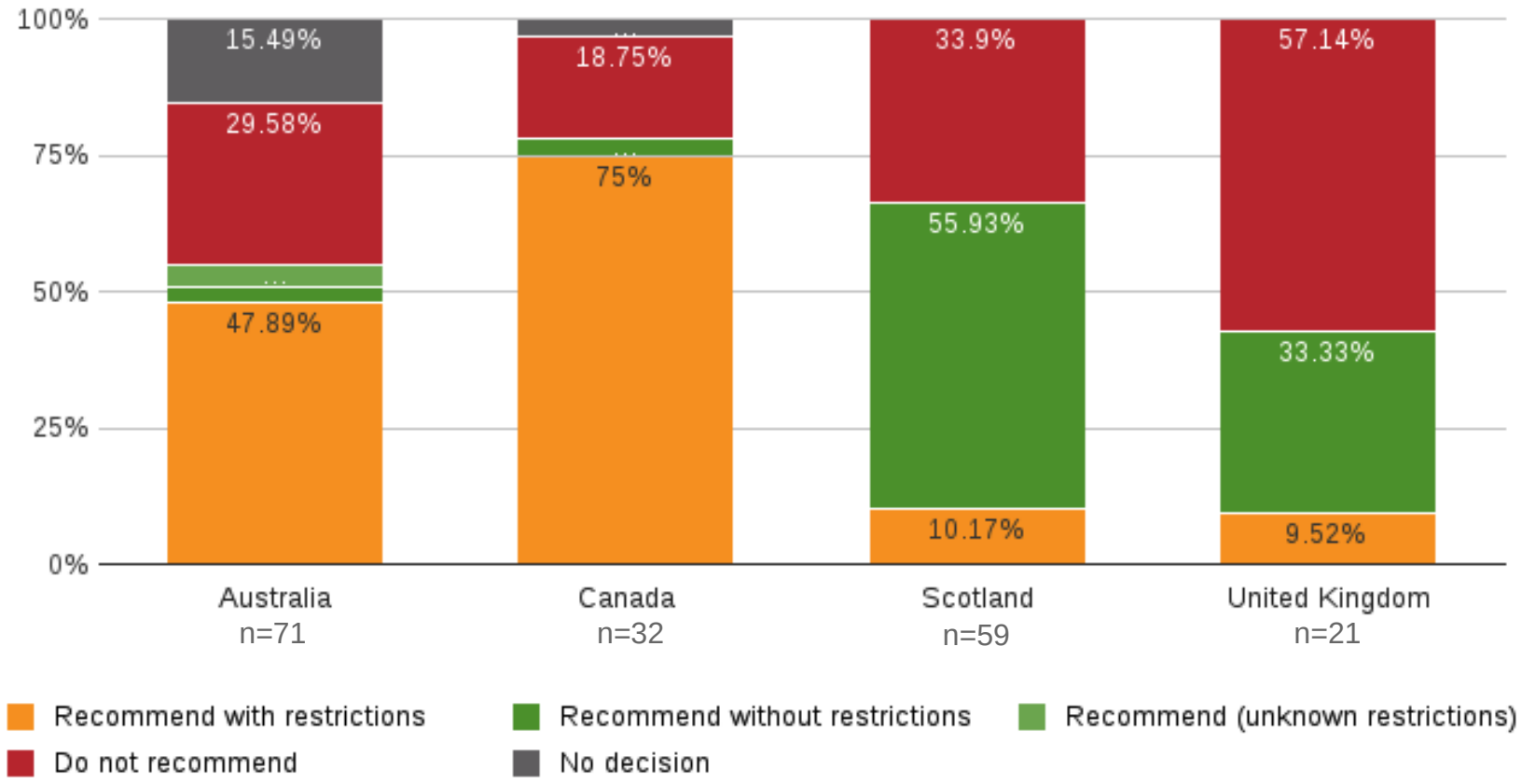
Be Greater Than

Source: Partnership to Improve Patient Care, 2017.
Measuring Value in Health Care: Uses and Misuses of the QALY

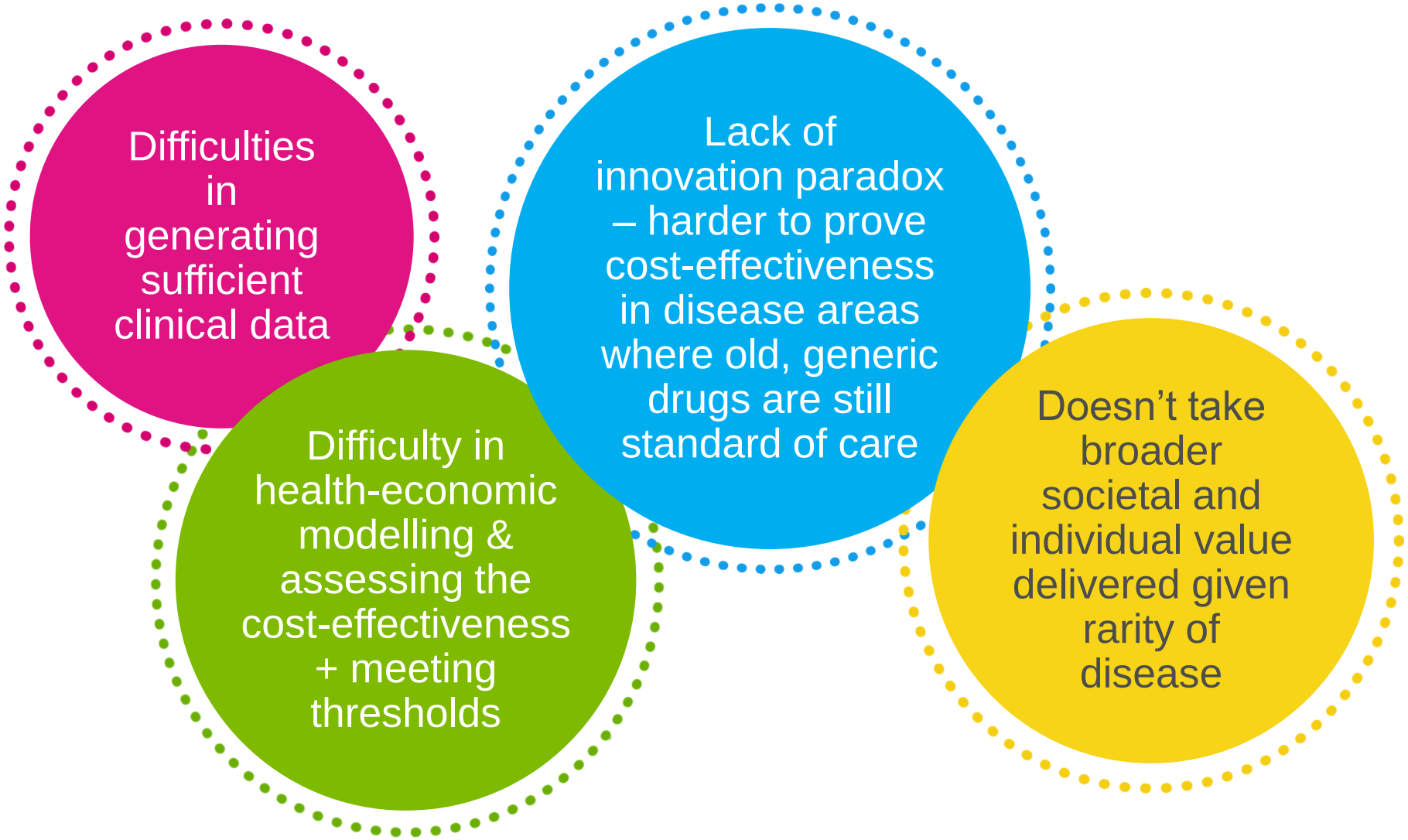
Impact of low, fixed cost-effectiveness thresholds in Oncology

Pfizer Oncology

Considering more criteria than cost-effectiveness alone & avoiding low thresholds leads to more oncology drugs being made available



Rare diseases face strong obstacles to reimbursement where cost-effectiveness thresholds are in place



HTA systems that primarily evaluate the clinical value for use in a pricing negotiation

A set of criteria, often including cost effectiveness, clinical benefit and severity of disease are used to rate a drug. Rating scale used in Germany:

- **A** Major extent of benefit
- **B** Considerable extent of benefit
- **C** Minor extent of benefit
- **D** Not quantifiable extent of benefit
- **E** No additional benefit shown
- **F** Benefits less than alternative

Rating then used in pricing negotiation but how exactly it relates to final price can lack transparency

Different HTA provisions made for orphan drugs

No Cost-effectiveness evaluation required if no alternative exists	Some form of safety net mechanism if drug deemed not cost-effective
NEL, IT & DE	DK, FR, UK, FI, NOR, SP, AUT, BE

Extent to which rare disease drugs are reimbursed varies and safety net mechanisms can face criticism for a lack of transparency & consistency of decision making

Short, H, et al, 2015. A National Approach to Reimbursement Decision-Making on Drugs for Rare Diseases in Canada? Insights from Across the Ponds. *Health Policy*, 10(4), 24-46.

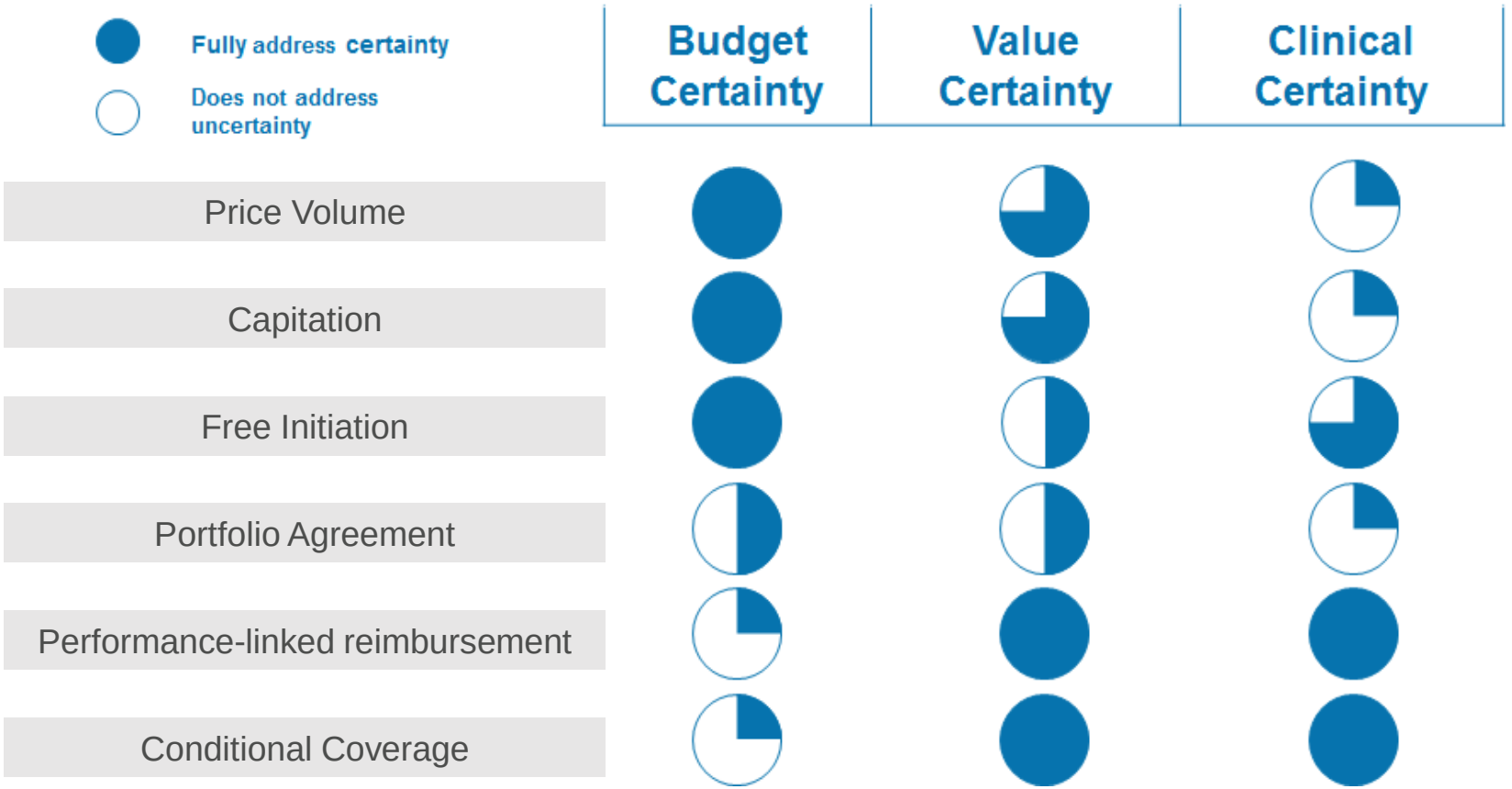
Managed Entry Agreements

An arrangement between a manufacturer & payer that enables reimbursement for a drug subject to specific conditions

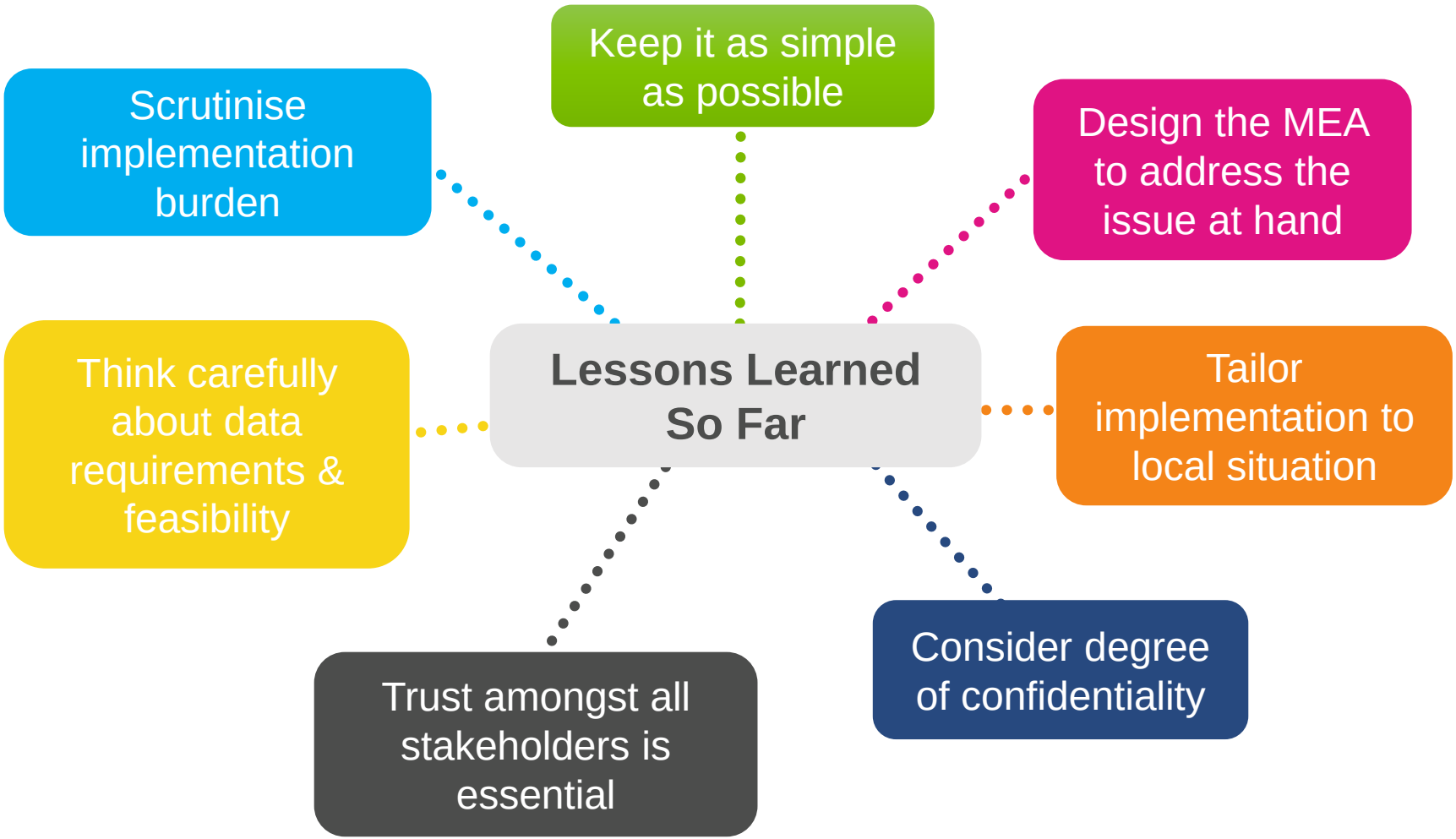
Use a variety of financial or patient outcomes-based mechanisms to address uncertainties about the performance of a drug

Managed Entry Agreements provide interesting options…..

The relationship between the type of scheme and the underlying cause of uncertainty

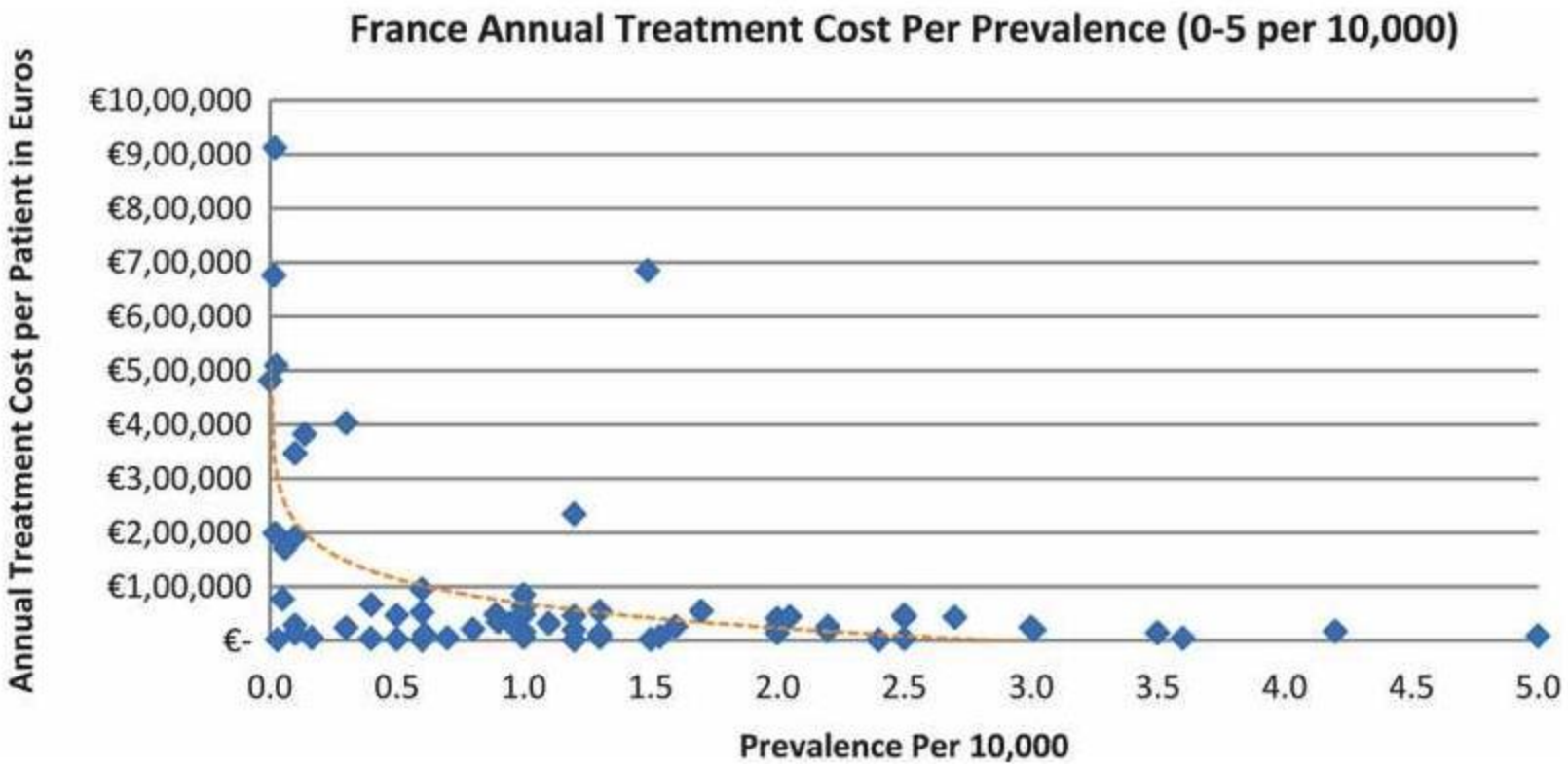


… but must be considered carefully by all stakeholders



Is Rarity valued by EU Payers? Yes, to some extent

study assessed relationship between the prevalence of rare diseases and the annual treatment cost of orphan drugs in selected EU countries



Medic, G, et al. 2017. Do payers value rarity? An analysis of the relationship between disease rarity and orphan drug prices in Europe. *Journal of Market Access Health Policy*, Apr 10;5(1)

Pfizer Innovative Health

Pfizer Oncology

Conclusions

Be Greater Than

Patients deserve all of our best efforts

Given high unmet patient need, all stakeholders need to collaborate to find ways to accelerate development, registration & access to new drugs globally

Such work underway – EMA & EU Healthcare Payers met recently

HTA considering broader factors than just cost-effectiveness will lead to greater access to new drugs for rare disease patients

Exploring Opportunities for Collaboration between Regulators & Payors. EMA Press Release, September 2017