



# THE NEW COURSE OF CLINICAL STUDIES IN EUROPE

XV FORESIGHT TRAINING COURSE  
BOOSTING RESEARCH AND INNOVATION IN A  
CHANGING REGULATORY FRAMEWORK

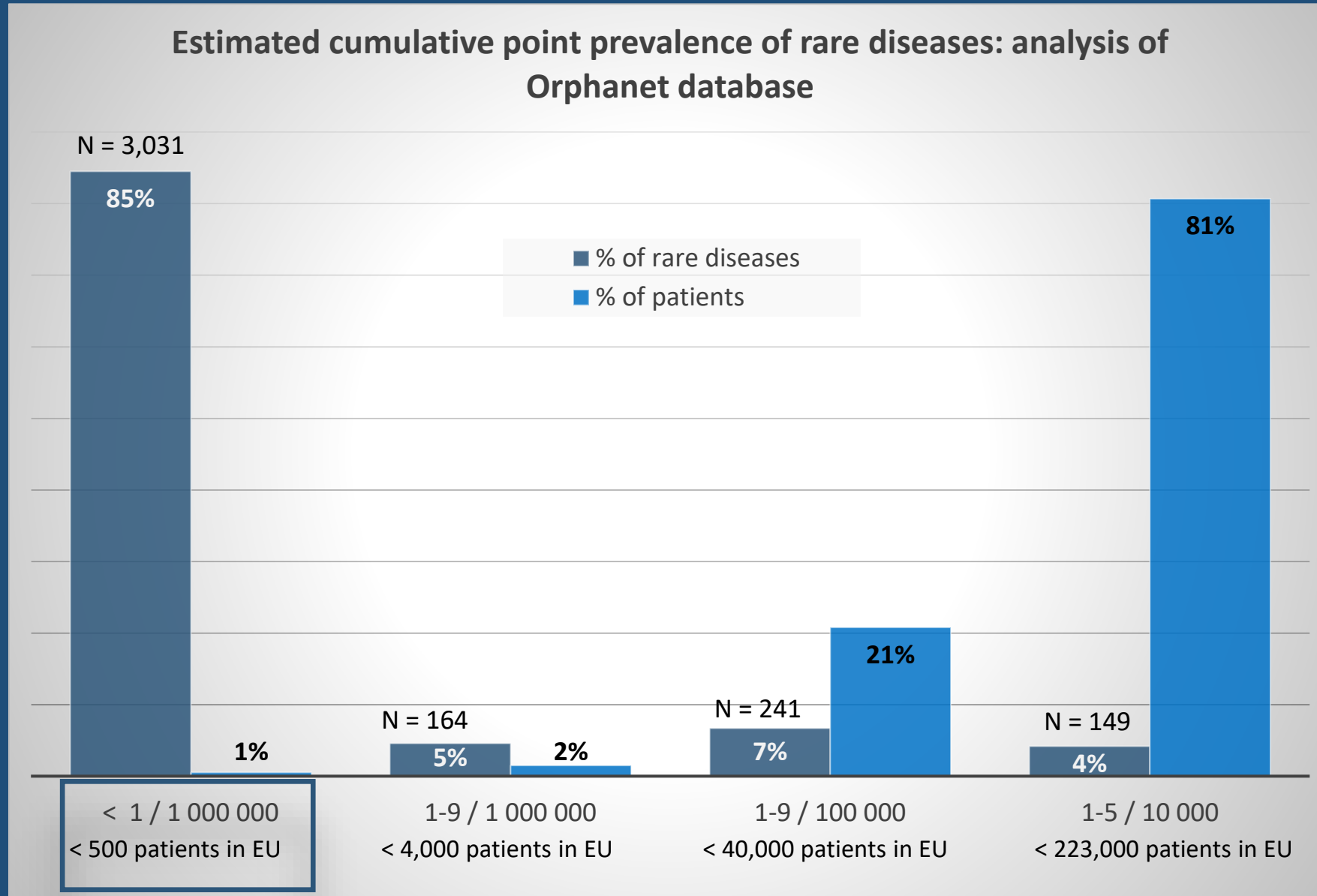
15-16 DECEMBER 2022, BARI, ITALY



- Innovation in methodologies for clinical research is nothing to be afraid of, and much more than an opportunity
- **It is a necessity**

- — the case of small populations

# The distribution of rare diseases by prevalence





RESEARCH

Open Access

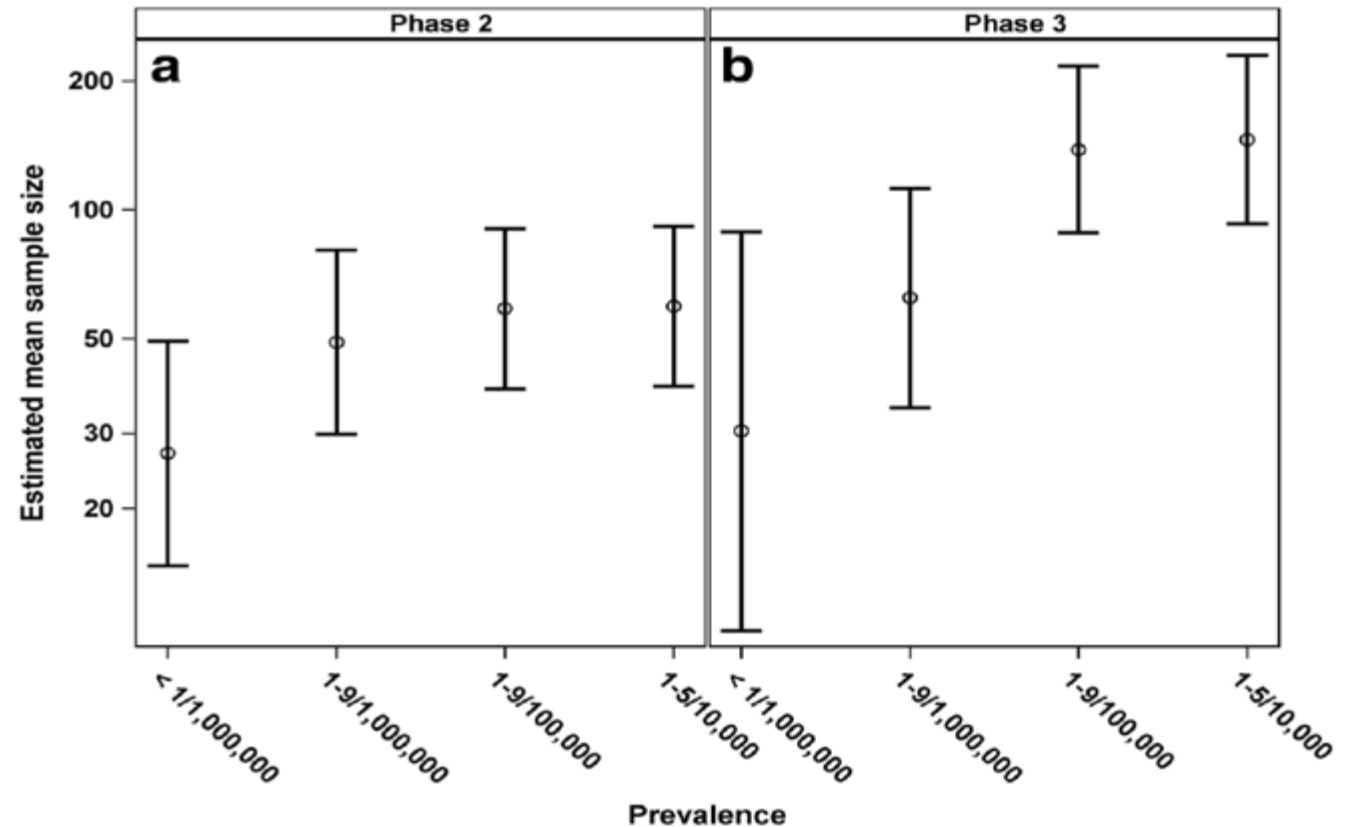


# Does the low prevalence affect the sample size of interventional clinical trials of rare diseases? An analysis of data from the aggregate analysis of clinicaltrials.gov

Siew Wan Hee<sup>1\*</sup>, Adrian Willis<sup>2</sup>, Catrin Tudur Smith<sup>3</sup>, Simon Day<sup>4</sup>, Frank Miller<sup>5</sup>, Jason Madar Sarah Zohar<sup>7</sup> and Nigel Stallard<sup>1</sup>

Presented by Olivier Collignon, PhD, on 16 April 2018  
EMA, National expert seconded from the Luxembourg Institute of Health

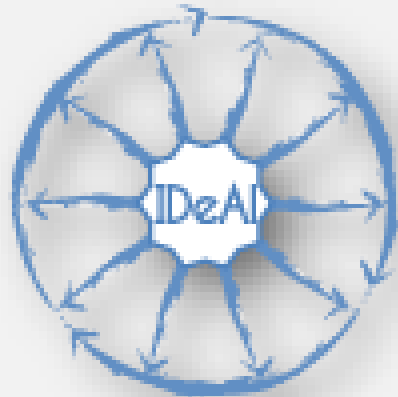
***"We found that there were very few multi-nation trials suggesting that the opportunities to conduct larger or 'adequately' size trials were underused."***





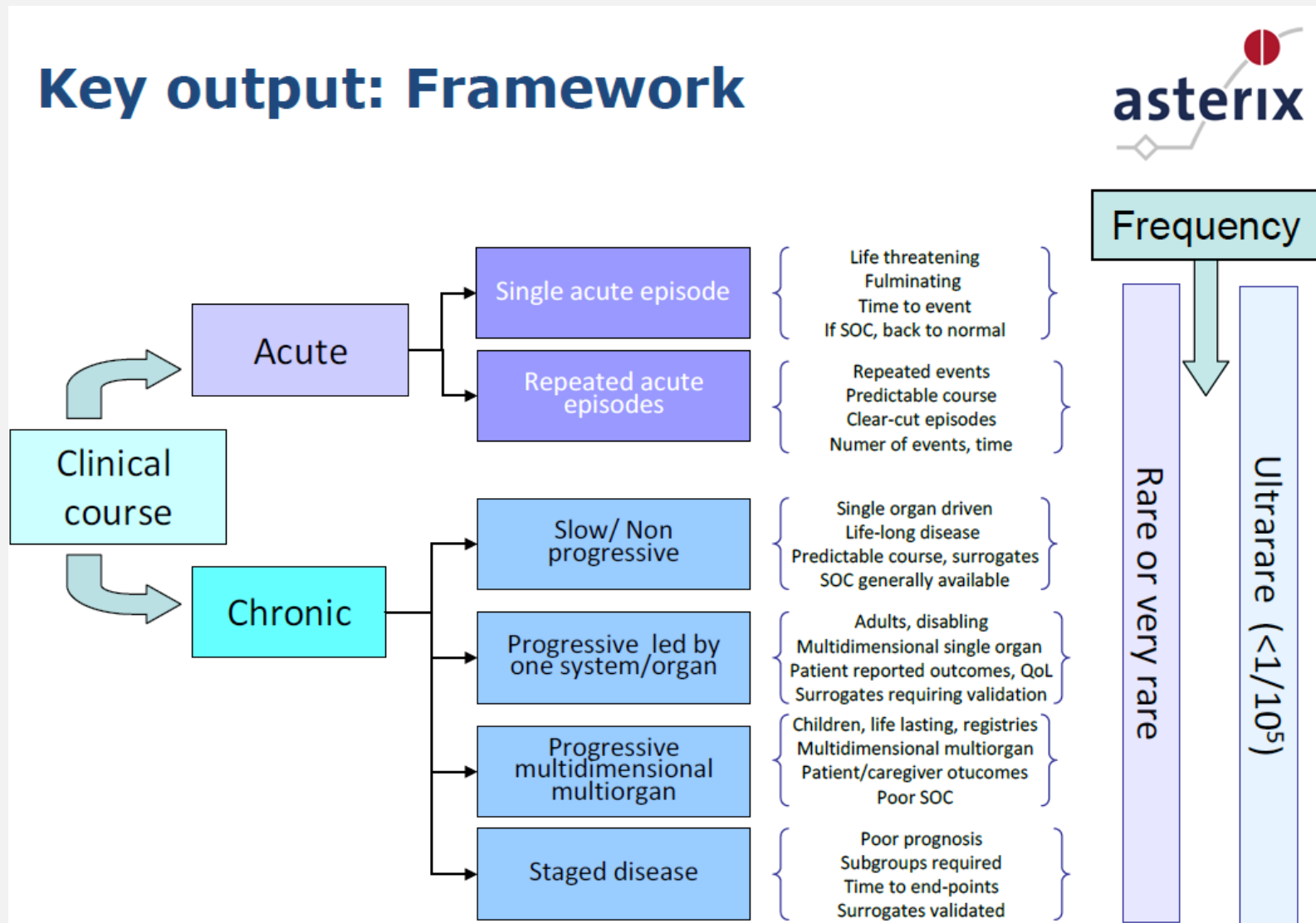
- Ronald A. Fisher published the statistical methods (F test) in his early book *Statistical Methods for Research Workers*, published in **1925**
- First published RCT in medicine: **1948**
  - —A gold standard that is almost one century old already

# Three EU FP7 dedicated to methodologies in rare diseases



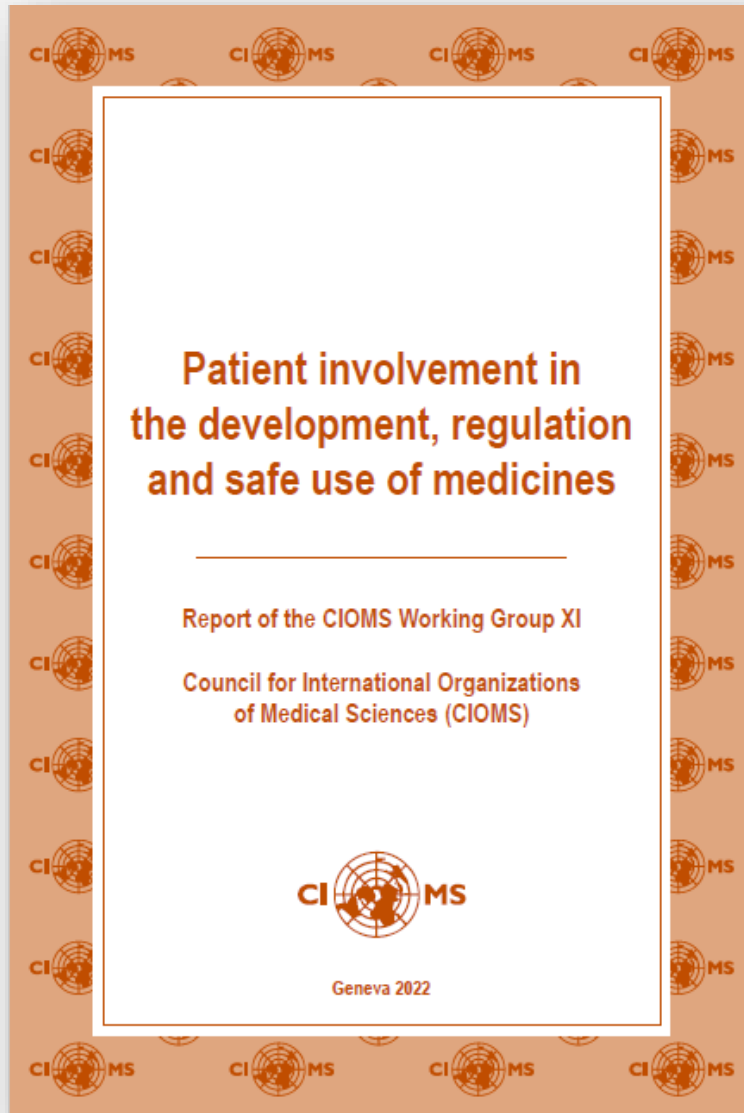
Integrated DEsign and AnaLysis  
of small population group trials

# Advances in Small Trials dEsign for Regulatory Innovation and eXcellence (ASTERIX) project



Project's principal investigators: Kit Roes and Armin Koch

<http://www.asterix-fp7.eu/>



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**Ethical considerations for patient involvement**

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**Executive summary**

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**Chapter 1: Introduction**

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**Chapter 2: Landscape**

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**Chapter 3: Guiding principles**

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**Chapter 4: Advancing treatments**

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**Chapter 5: Use of real-world data and evidence**

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**Chapter 6: Product labeling**

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**Chapter 7: Rapid safety communication**

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**Chapter 8: Additional risk minimization**

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**Chapter 9: Clinical practice guideline**

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**Chapter 10: Low- and middle-income countries**

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**Chapter 11: Pandemic considerations**

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**Appendices:**

- 1. Glossary**
  - 2. Case studies**
  - 3. CIOMS WG XI statement**
  - 4. CIOMS WG membership and meetings**
  - 5. List of commentators**
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# Chapter 1. Introduction

## 1.1 Terminology

Opportunities to incorporate the patient's perspective

## 1.2 Increasing engagement and incorporating the patient's perspective

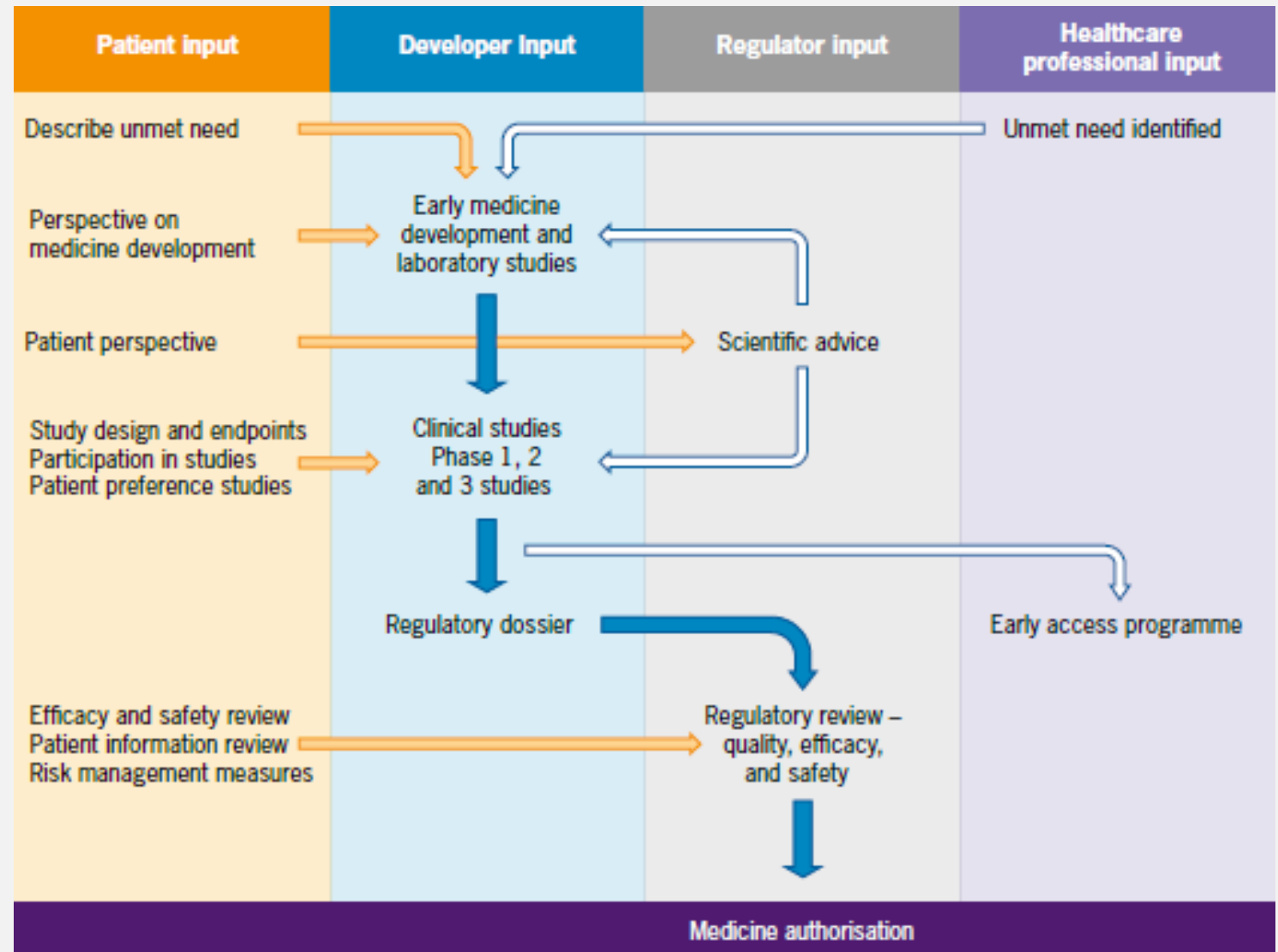


Figure 1a: Patient involvement during a medicine lifecycle: **pre-authorisation**



# THANK YOU!

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# Not all patients eligible: Therapeutic window

