Advancing Molecular Diagnostics for Oncology:

Partnerships to Accelerate Evidence Development

Assessing Clinical Utility with Real-World Evidence

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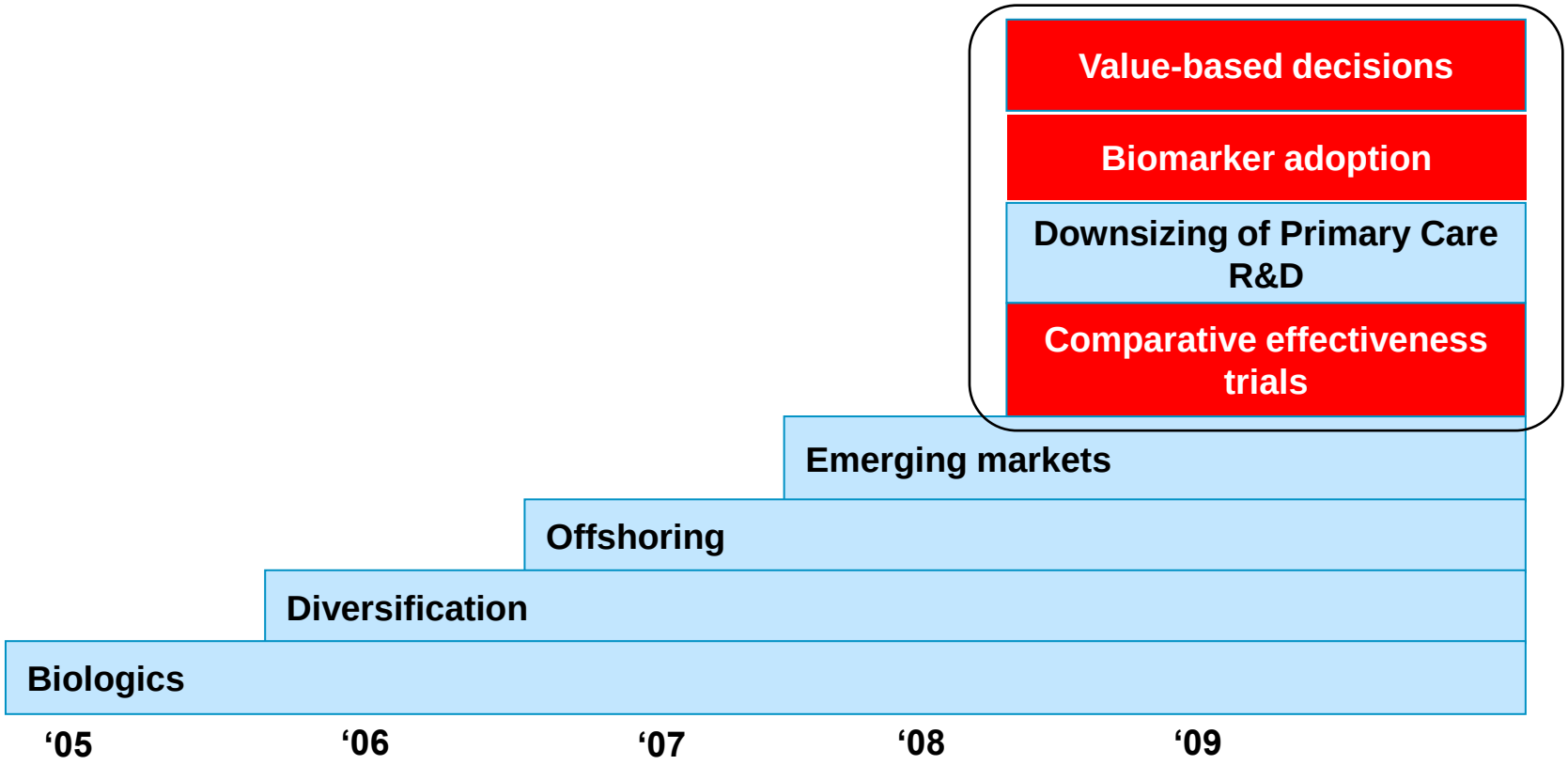
Legal Disclaimer

The information presented here is intended to facilitate debate and is not meant to be promotional in any fashion.

“no problem has a final solution; every solution is an admission ticket to another problem”

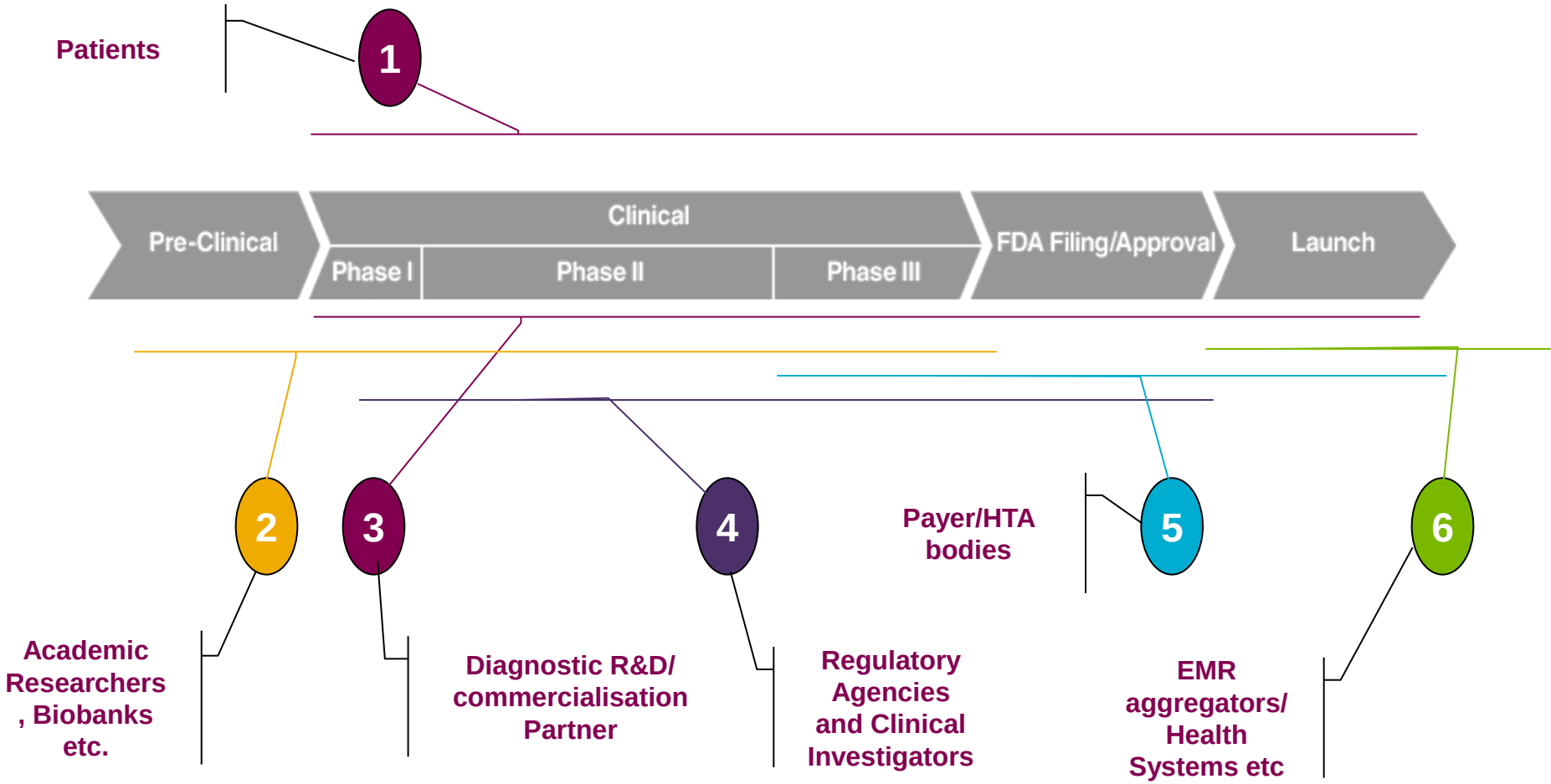
Henry Kissinger
TIME interview June 6 2011
http://www.time.com/time/magazine/article/0,9171,2074215,00.html

The Changing Rx/Dx Model



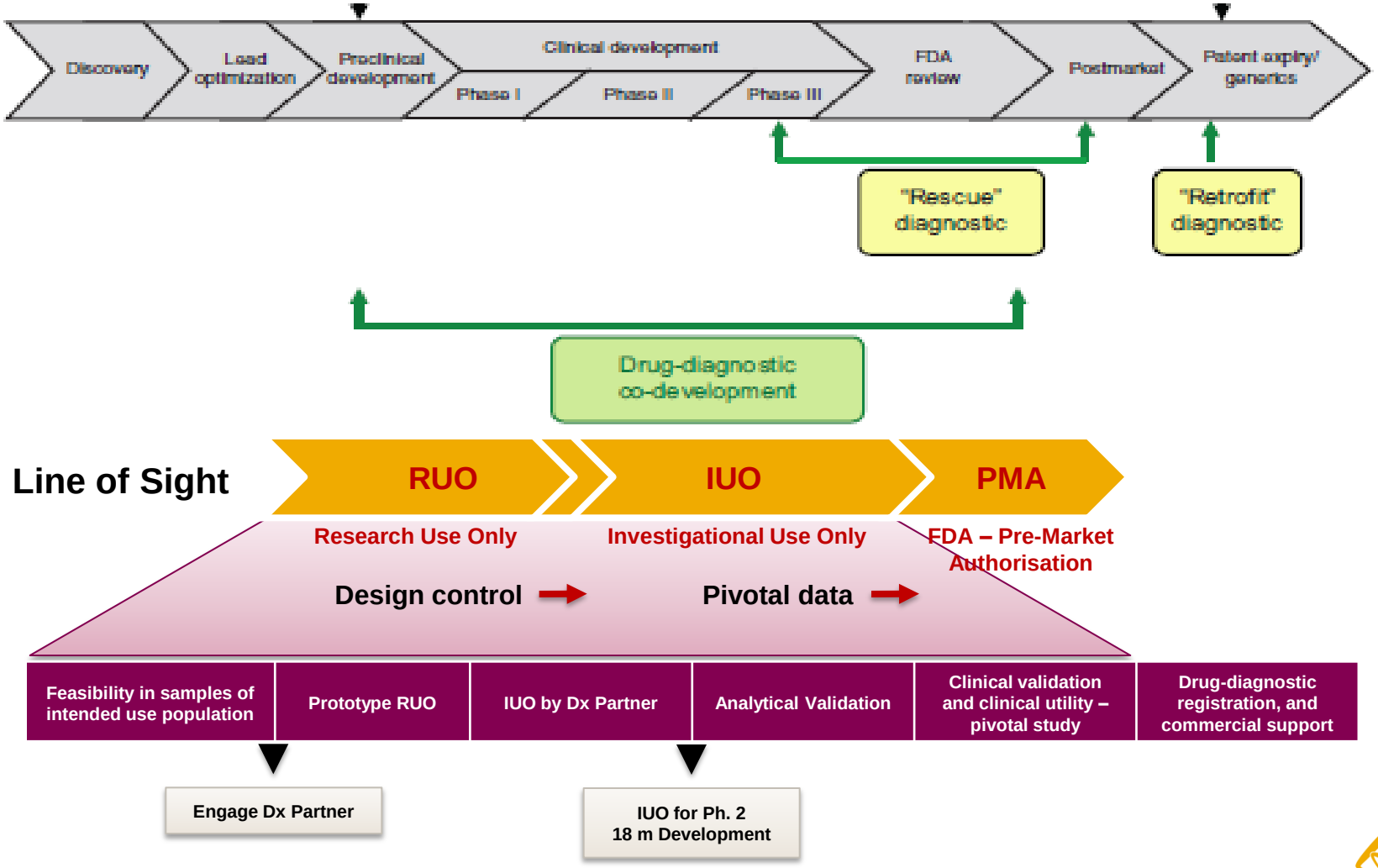
From Morgan Stanley report

Developing Companion Diagnostics Partnerships...



Categorization of Companion Diagnostics

CD with clinical validity and utility demonstrated at Launch is at initial launch remains challenging



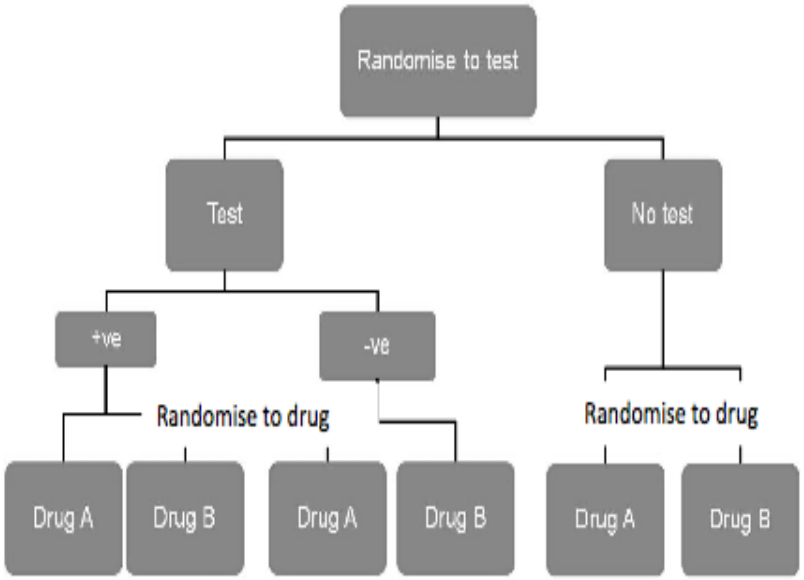
Adapted from Woodcock, J. 2010 Clin Pharm Therapeutics 88;6 pp765-773

Australian 2010 Draft for Consultation Document

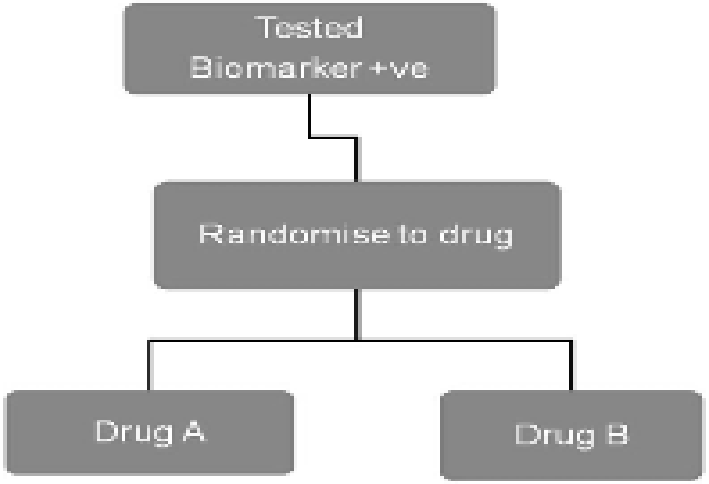
The draft specified over 70 specific questions regarding HTA for co-dependent technologies

Evidence Development Strategies

Level 1:
Double Randomised Trial



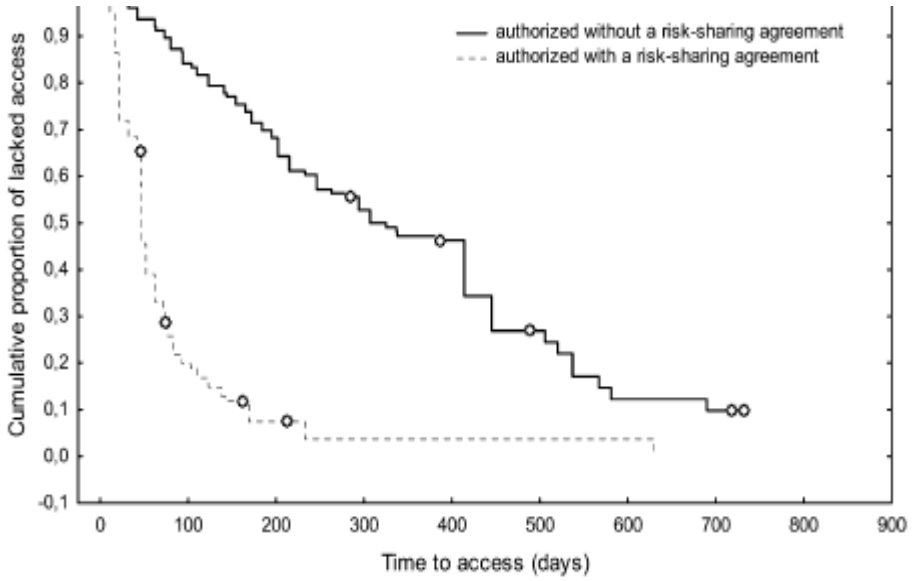
Level 3:
Randomised trial of drug only (with the eligibility of all subjects determined by test result)



Italian (AIFA) Specialty Product Registry

Italian Managed Entry schemes have managed utilization, provided evidence on use patterns and outcomes and driven timely access of high cost oncology therapeutics

Kaplan–Meier curve of regional patient access to oncology products approved by the EMA from 2006 to 2008 in Italy



"Time to market and patient access to new oncology products in Italy: a multistep pathway from European context to regional health care providers," P. Russo, F. S. Mennini, P. D. Siviero & G. Rasi, Annals of Oncology, March 24, 2010

Clinical Utility

ACCE definition

The balance of benefits and harms associated with the use of a test in practice, including improvement in relevant outcomes and the usefulness of added value in decision making compared with not using the test

RWE role in Clinical Utility assessments in Oncology

Challenges re EMR and Claims databases studies

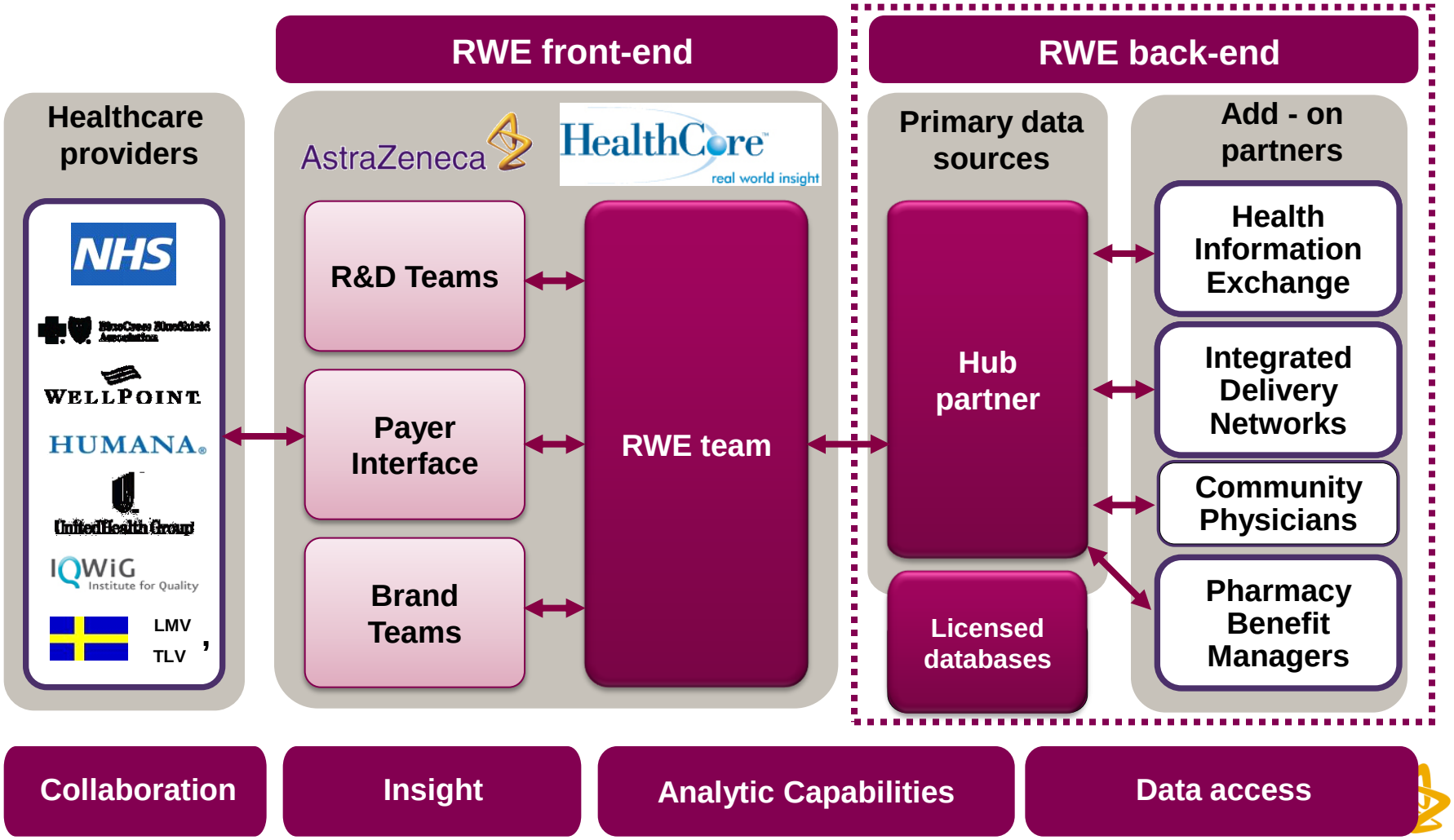
- **Patient characterization**
  - lack of integrated data on important pt clinical characteristics, as well as pathologic and diagnostic data
- **Outcome assessments**
  - lack of data/consistency on imaging, assessment timing, concordance, PROs...
- **Cost outcomes**
  - Difficulty collating all associated direct and consequential costs
- **Clinical context re Tx and Dx decisions**
  - semantic interoperability challenges, confounding by indication bias
- **Continuous longitudinal records**
  - segregated data re site of care and data richness across databases (eg detailed insight into process, treatment and outcomes (esp AEs) during hospital stays)

RWE role in Clinical Utility assessments in Oncology
What can we do with RWE today?

- **Assess Process of Care**
  - Monitor practice patterns pre and post technology introduction
  - Compliance with treatment recommendations/guidelines
  - Monitor (total) cost impact
- **Assess External Validity**
  - Assess generalizability through comparisons of high level clinical outcomes with prior intervention trials (RCT or PCT) evidence
- **Inform Comparative Effectiveness/Clinical Utility**
  - Generate hypotheses re putative benefits/risks of competing options/strategies (eg through patient level and/or site level comparisons)
  - Not yet ready for use as confirmatory evidence unless through specifically designed prospective registries.

Real Worlds Evidence Alliance

Linking EMR, Claims, pathology and diagnostic data may advance our understanding of Clinical Utility



Final Thoughts

What can we do with RWE today?

- **Apply general framework for clinical utility through interventional trials (RCT and PCTs) - but – allow judgment on level of evidence required eg accelerated access for promising technologies**
- **Use observational/database analyses today to augment interventional study data to assist managed entry**
- **Use "enlightened community" concept to build integrated, outcomes based databases to better understand external validity, inform unmet need assessments/trial designs and identify variation in practice/hypotheses for detailed interventional studies**
- **Establishing an environment to allow pre competitive collaborations and data sharing to enable emerging biomarker data to enrich our research databases and therefore understanding of practice patterns and clinical outcomes in the real world setting**

Partnerships are fundamental to propel us towards a learning healthcare system…