Personalized Healthcare and Health Technology Assessment

Jens Grueger, PhD
Vice President, Head of Global Pricing & Market Access, Roche Pharma AG

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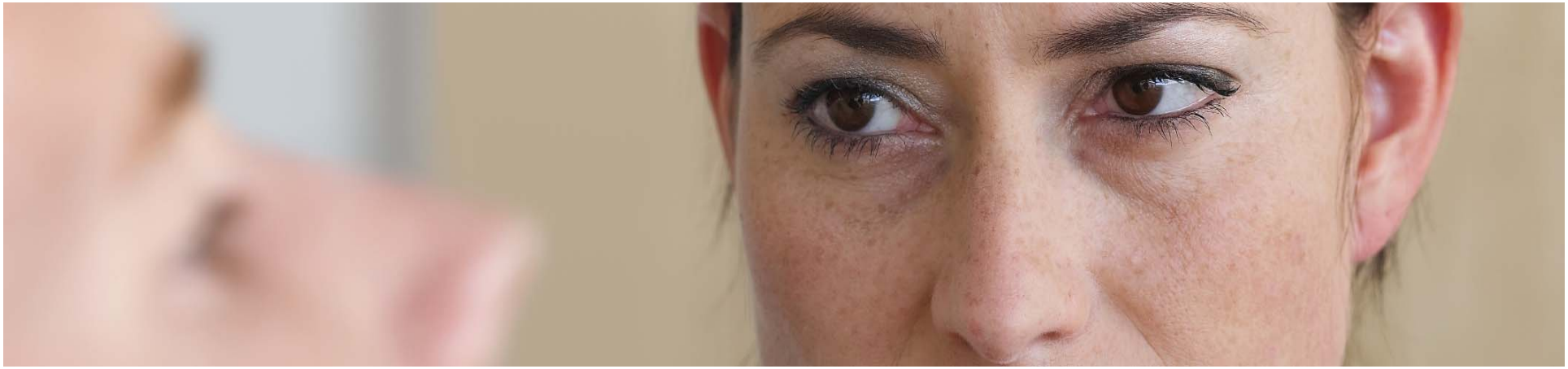

Roche

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Evidence for Personalized Healthcare

Personalized reimbursement models

Conclusions

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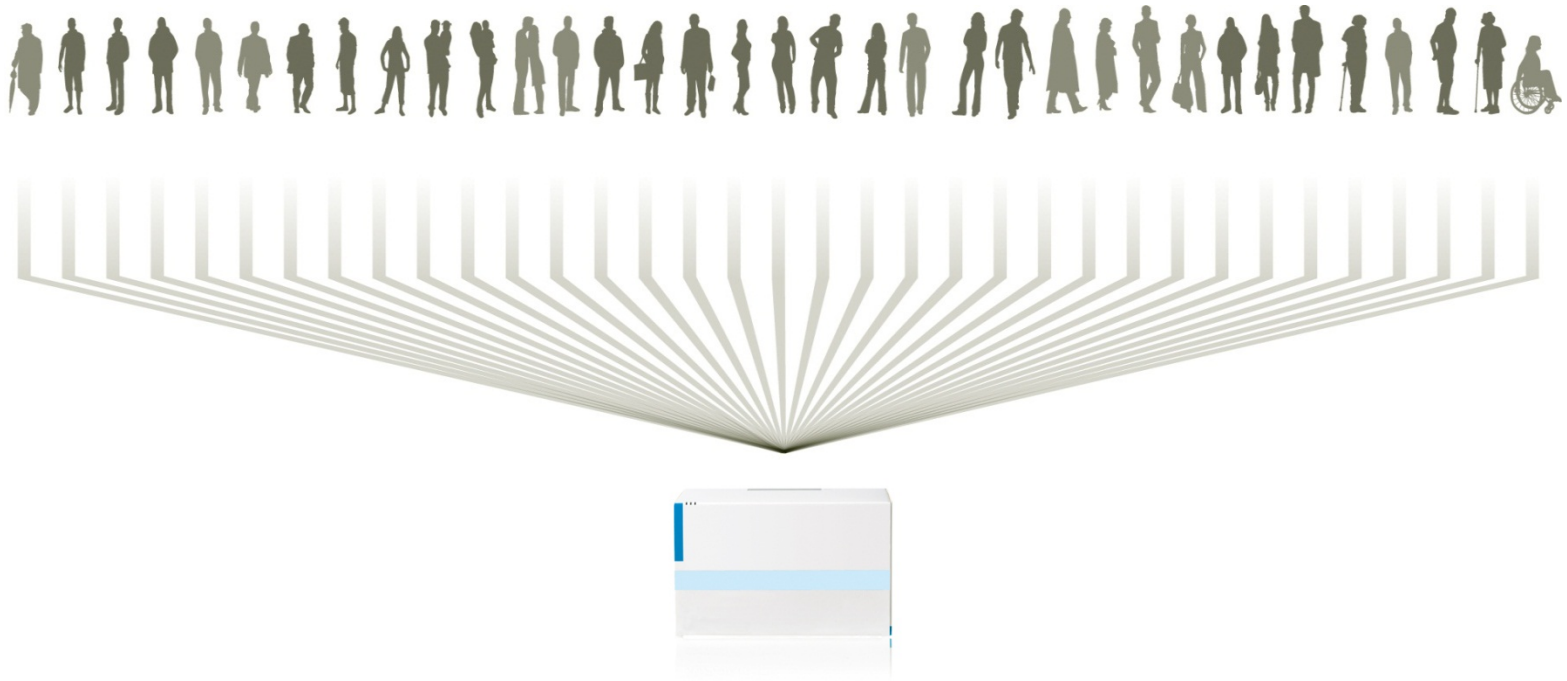
We are in the transition from the “blockbuster model” …

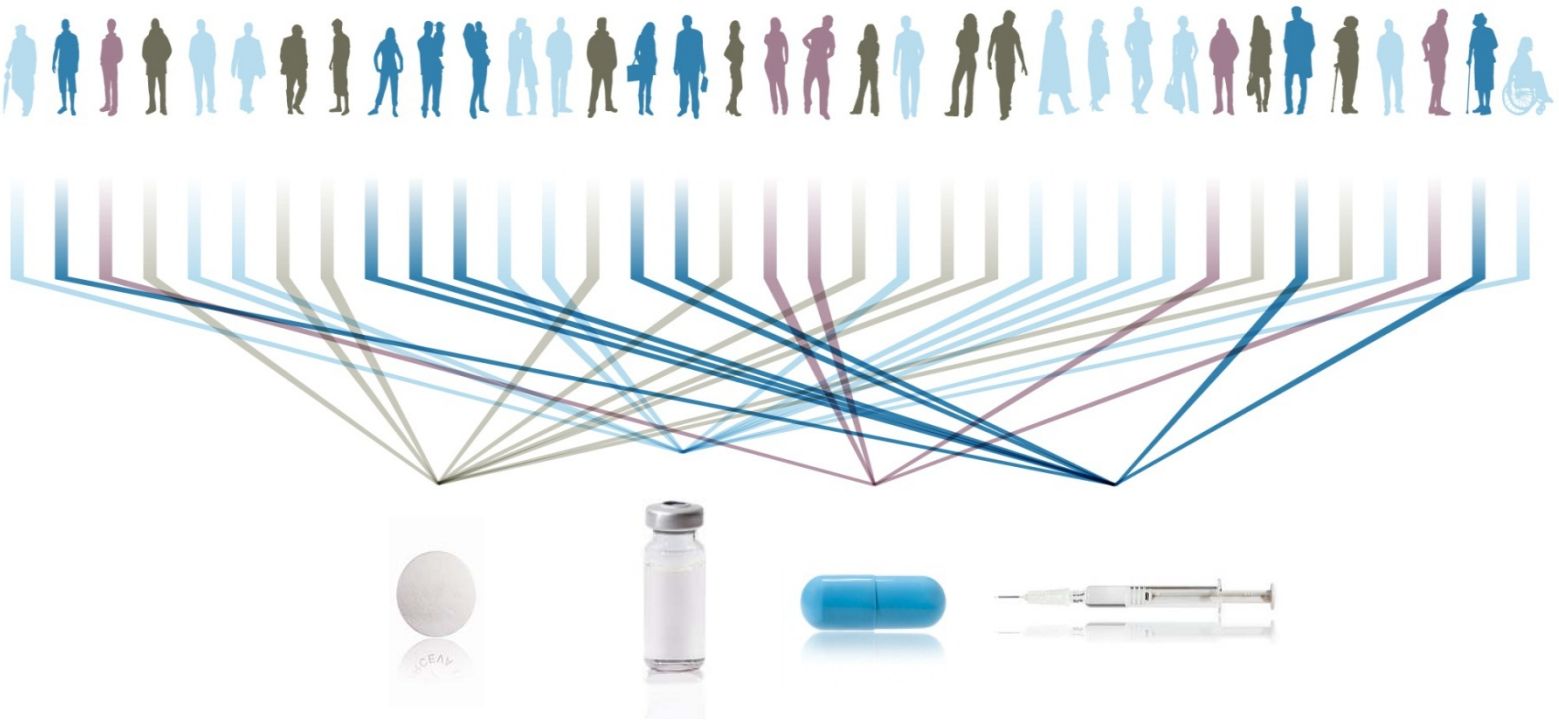
Patients with same syndrome



One-size-fits-all approach

.. to a Personalised Healthcare model

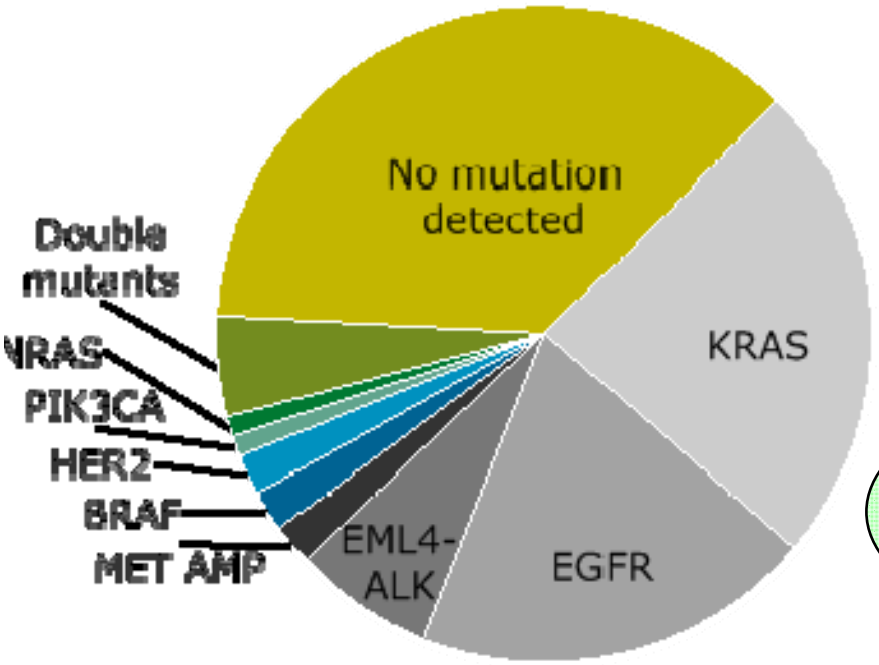
Group of patients with the same syndrome



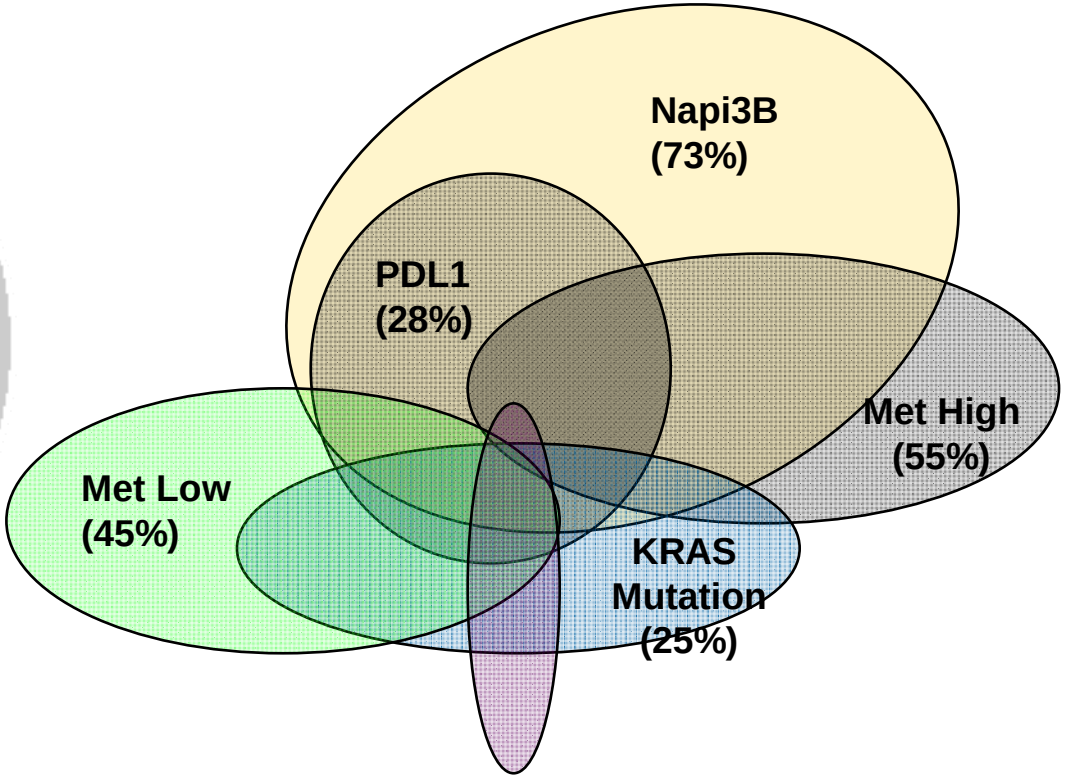
Targeted therapy

Scientific advances in cancer increasingly allow targeting the disease with the right (combination of) mechanisms

Potential driver mutations (NSCLC)



Overlapping Biomarkers (NSCLC)



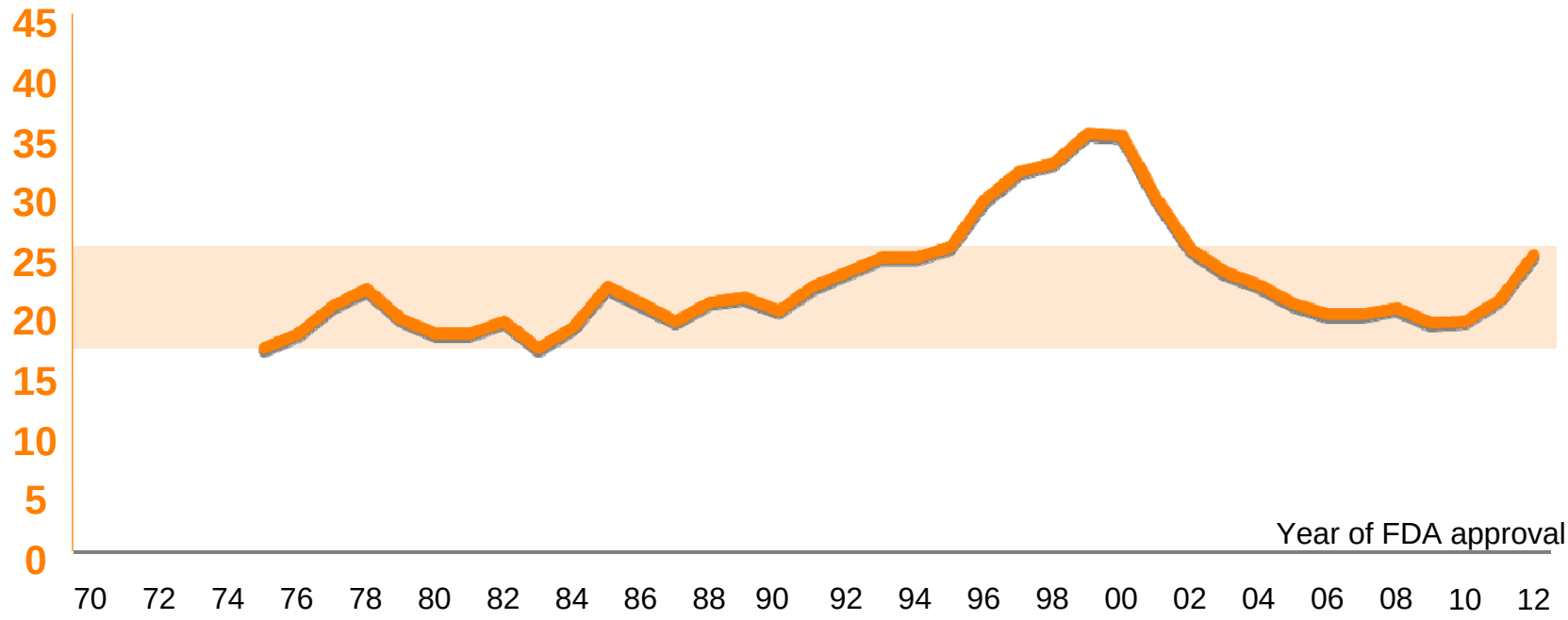
Co-dependent technologies in Oncology

- 13 drugs against 7 targets
- 6 of these in the last 24 months
- R&D presentations indicate that there are many more co-dependent technologies in the pipeline

Date	Drug	Markers
1998	trastuzumab	HER2
2001	imatinib	BCR-ABL, KIT
2004	cetuximab	KRAS
2006	dasatinib	BCR-ABL
2006	panitumumab	KRAS
2007	lapatinib	HER2, EGFR
2007	nilotinib	BCR-ABL
2011	crizotinib	EML4-ALK
2011	vemurafenib	BRAF
2012	pertuzumab	HER2
2012	bosutinib	BCR-ABL
2012	ponatinib	BCR-ABL
2013	trastuzumab emtansine	HER2

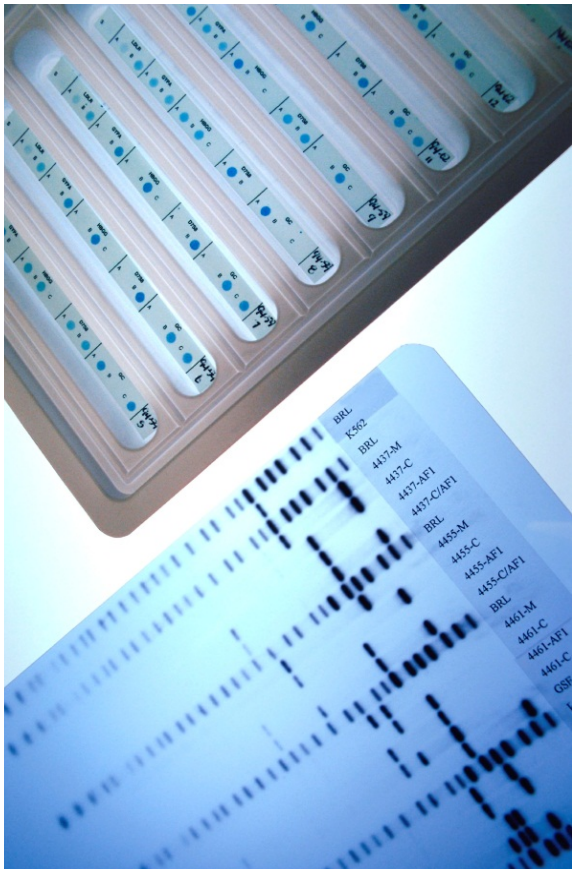
Progress of Science
Signs of recovery?

 # New Molecular Entities
(moving 5 year average)



Source:. NME data for 1966-1971 from Peltzman, S. (1973) J. of Political Economy 81, no. 5: 1049–91. NME data for 1972-1979 as reported in Hutt, P.B. (1982) Health Affairs 1(2) 6-24. NME Data for 1980-2007 from Parexel's Pharma R&D Statistical Sourcebook. NME Data for 2008-2012 from FDA.

In a personalized healthcare setting, we need a differentiated model of value



- Medicines will have a different benefit depending on the specific mechanisms that underlie the disease pathology in a patient
- Diagnostic procedures will detect different targets with different characteristics (sensitivity and specificity)
- Optimal patient outcome under real world conditions will require an aligned combination of diagnostics, medicines, outcomes measures and patient treatment pathways

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Health technology assessment

- HTA is a multi-disciplinary field of policy analysis, studying the medical, economic, social and ethical implications of development, diffusion and use of health technology *)
  - Always includes a systematic review of the clinical evidence
  - In many countries involves formal economic evaluation
  - Ethical and legal aspects are often ignored
- Distinction between
  - Assessment: scientific review
  - Appraisal: decision making

*) International Network of Agencies for Health Technology Assessment (INAHTA). http://www.inahta.org/HTA

HTA is everywhere

- Comparative effectiveness research and PCORI in the US, AMCP format for formulary submissions used by private payers
- Benefit risk assessment and quantification of “relative efficacy/effectiveness” by regulators (EMA)
- Qualitative assessment of clinical benefits eg France (ASMR) and Germany (Rapid Benefit Assessment)
- Characterization of level of innovation in Japan and Italy
- HTA including economic evaluation used in UK, Canada, Australia, the Netherlands, Sweden, South Korea

Conceptually PHC aligns with the goals of HTA

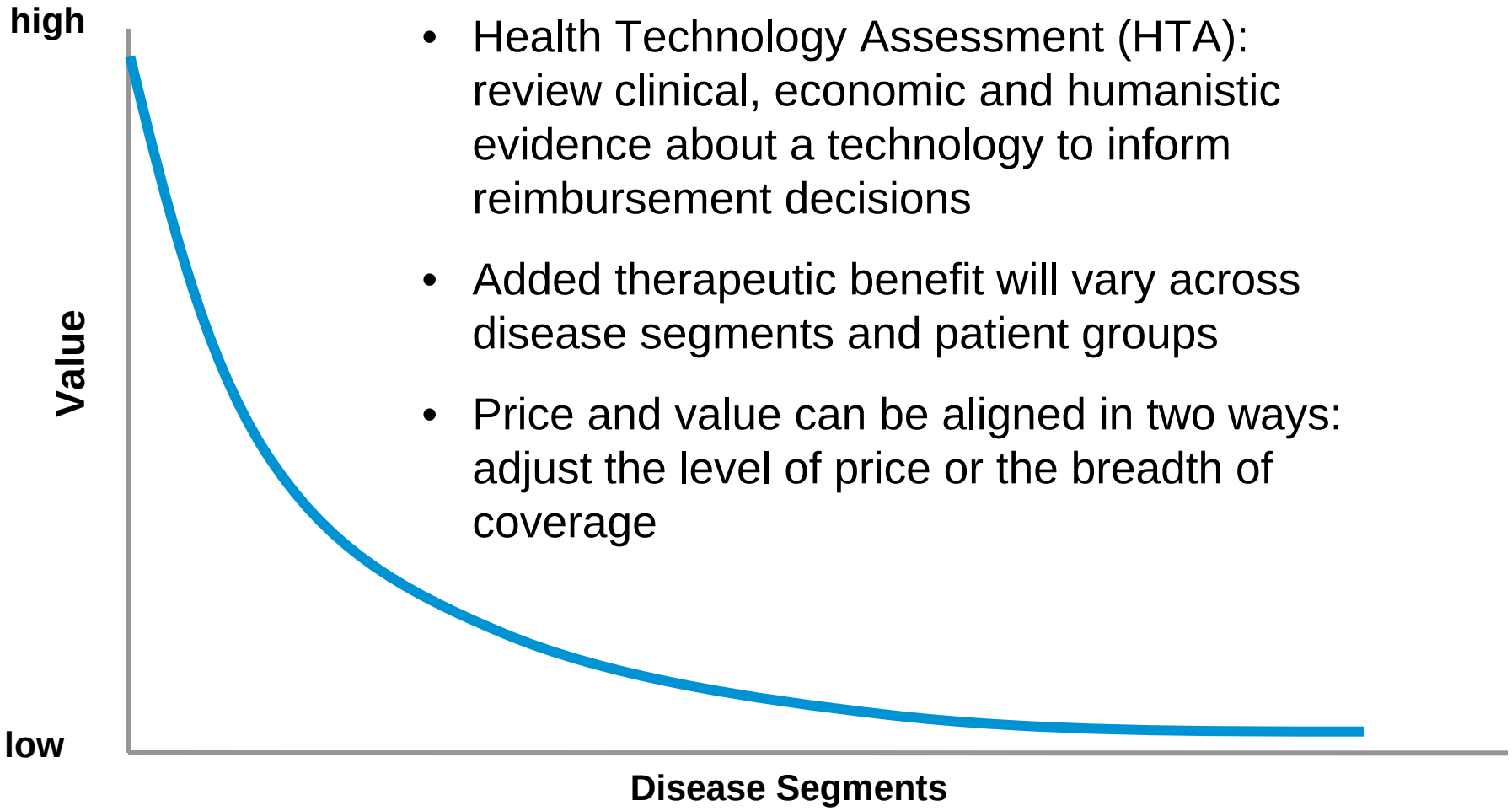
- To deliver better, safer, more effective treatments
- To better understand disease diversity or subtypes
- To identify the differences between patients and disease segments
- To identify the best drug targets
- To improve the quality and efficiency of R&D results

- Better and more predictable clinical and patient outcomes
- Improved mortality, morbidity and quality of life
- Fewer unnecessary treatments / side effects and associated costs
- Better compliance due to better results
- Optimized use of resources in healthcare

HTA promotes value-based pricing

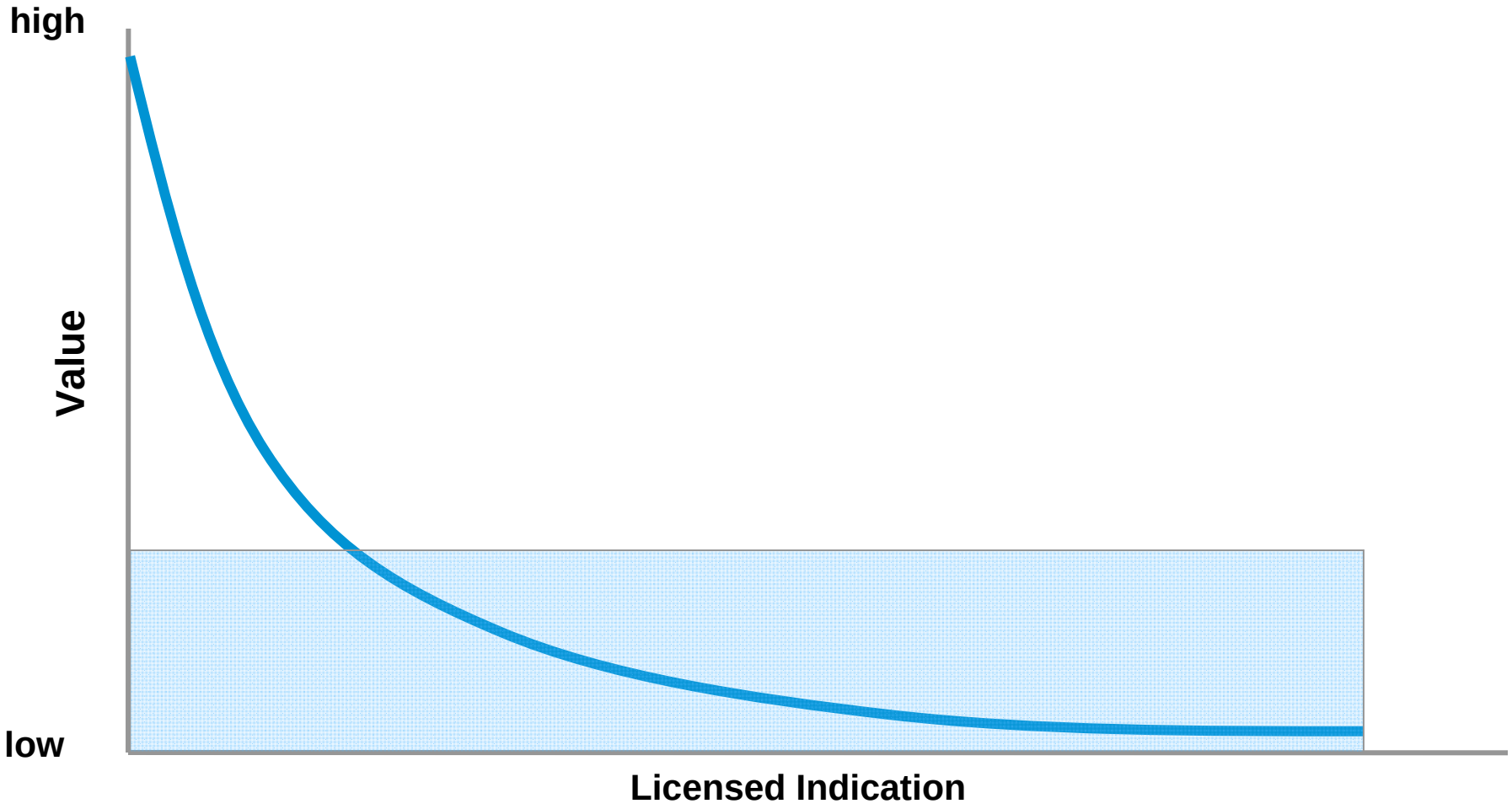
- In an HTA framework, a value based price is the sum of
  - Price of the therapy that we are replacing
  - Savings in the treatment pathway (reducing complications and side effects)
  - Value of the clinical benefits (improved survival, morbidity and quality of life)
  - Efficiencies in the healthcare system (easier administration, less monitoring)

Value based pricing is in line with payer demands

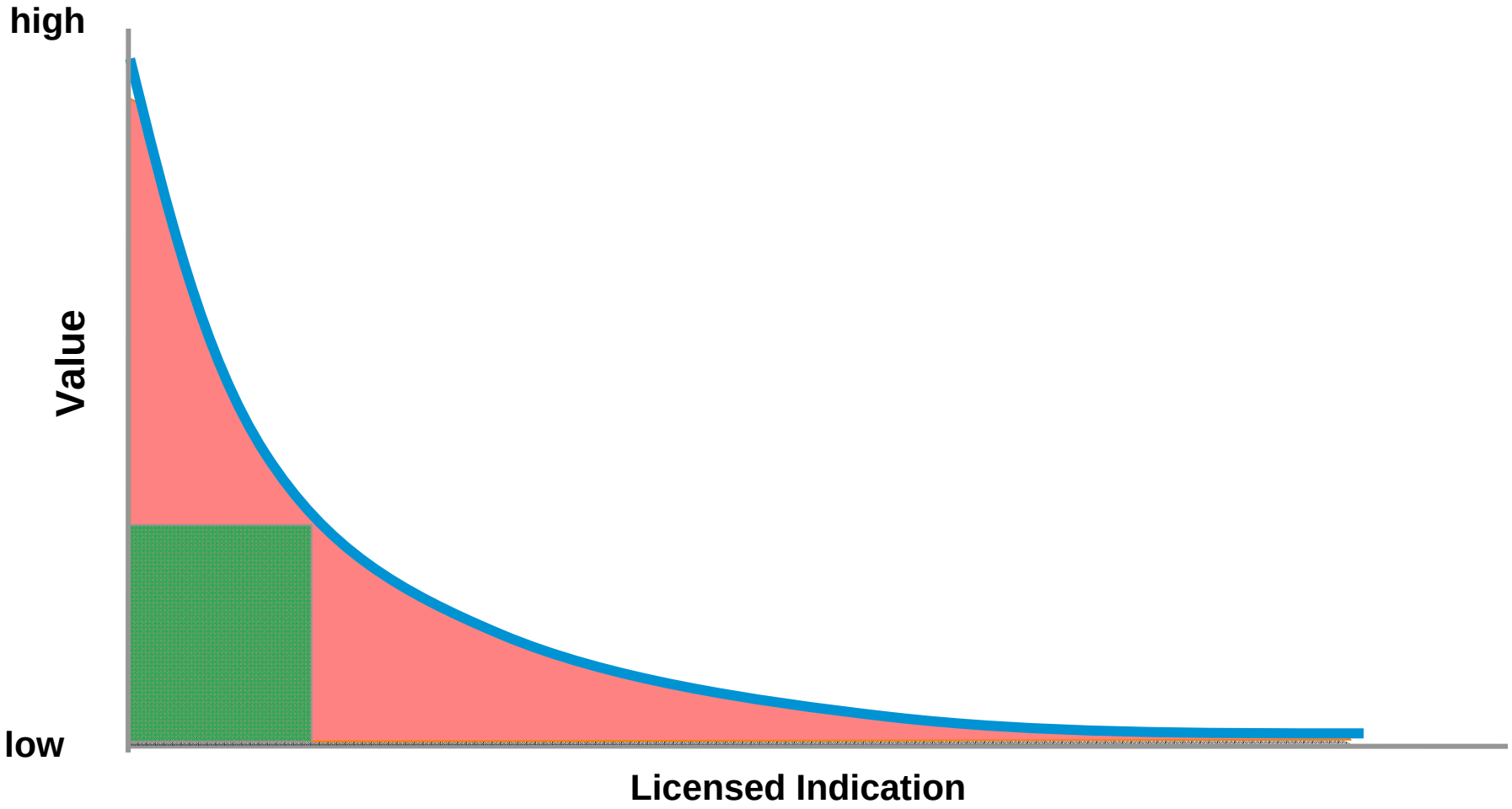


- Health Technology Assessment (HTA): review clinical, economic and humanistic evidence about a technology to inform reimbursement decisions
- Added therapeutic benefit will vary across disease segments and patient groups
- Price and value can be aligned in two ways: adjust the level of price or the breadth of coverage

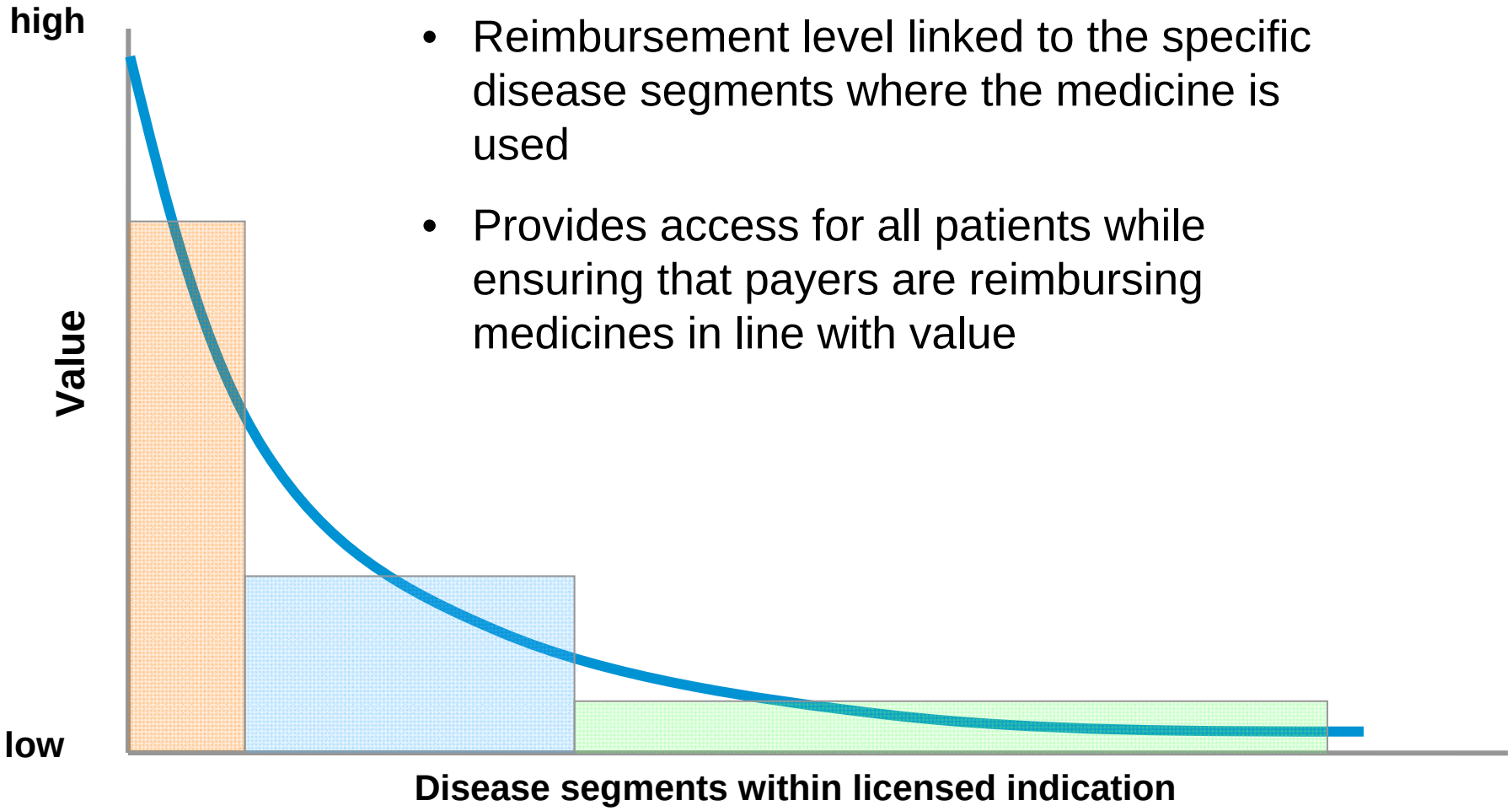
Traditionally, an “average” price was granted across the licensed indication



But then utilization was increasingly limited to the disease segment where the value is higher than the average



In a Value Based Pricing environment reimbursement should be linked to the specific utilization



- Reimbursement level linked to the specific disease segments where the medicine is used
- Provides access for all patients while ensuring that payers are reimbursing medicines in line with value

Critical questions for technology assessment and reimbursement in a personalized healthcare setting

- Assessment of added therapeutic value – different across disease segments
- Identification of disease segments will depend on diagnostic technology
- Pricing & reimbursement: value based price will vary across disease segments
- Efficacy vs effectiveness: needs to be assessed both at the medicine and the diagnostic level

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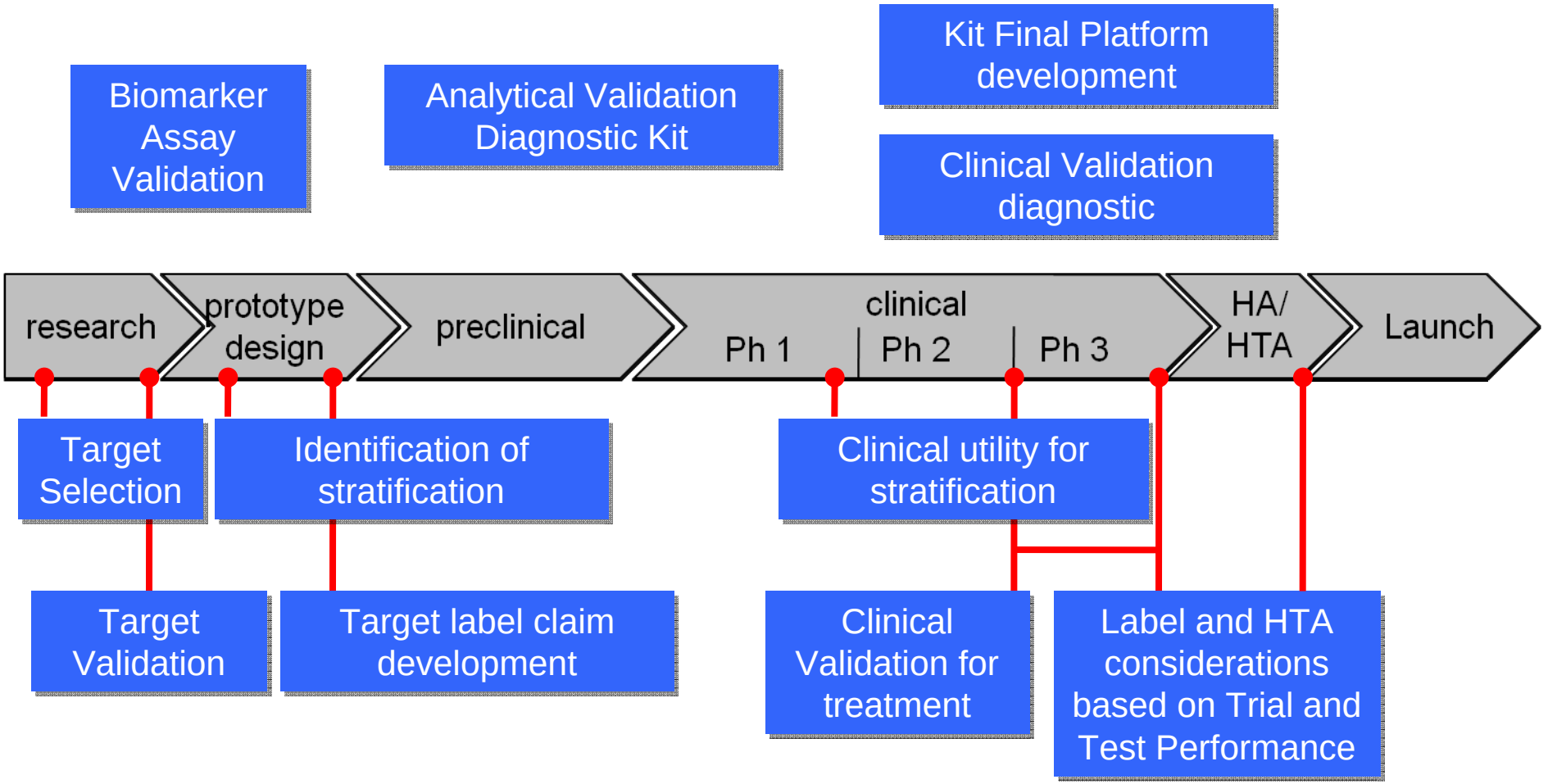
Ideal Co-development of Drug and Diagnostic

However, many times, confirmatory biomarker information will emerge after initial phase 3 program

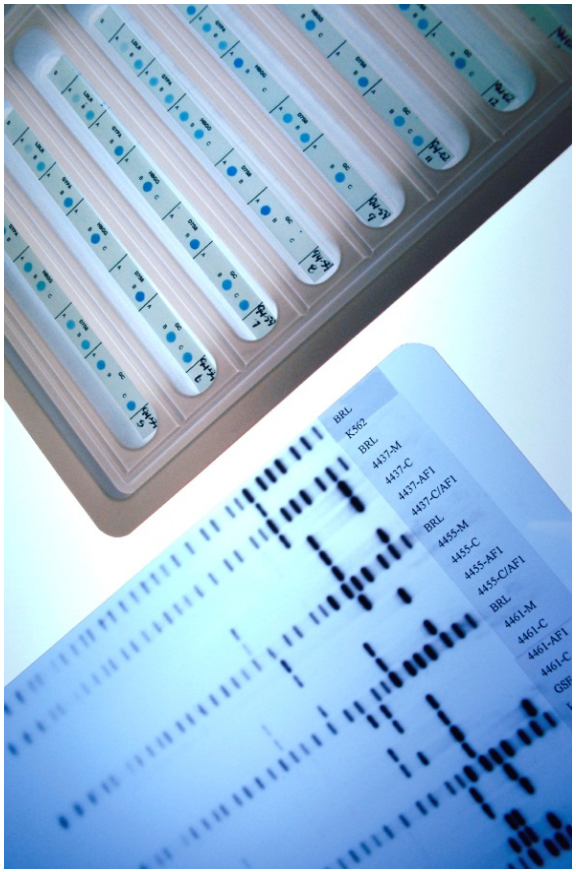


In 2011, Australia became 1st country to introduce a co-dependent HTA process

- Involves two or more technologies, such as a diagnostic test and a drug funded under different programs (e.g. MBS and PBS)
  - "Health technologies are co-dependent if their use needs to be combined … to achieve or enhance the intended clinical effect of either technology. For example, a drug/test combination where a new medicine seeking listing on the PBS may have a related pathology test that helps to determine the population group for that medicine"1
- New MSAC process has pre-submission step which increases timelines and may impact on PBAC submission dates
- Process starts with the decision question (PBAC submissions start with the answer)

[1] *Source:* *http://www.health.gov.au/internet/hta/publishing.nsf/Content/co-1*

In a personalized health care environment the evidence for the diagnostic and the medicine need to be assessed jointly



- Each diagnostic test will have its specific characteristics and identify different disease and patient segments
- Where a standard diagnostic has been established, or the new diagnostic is developed in parallel with the medicine, this is the natural combination to be included in the clinical trial
- Who is responsible for providing the evidence where different manufacturers/sponsors are involved?

Example: Vemurafenib in BRAF+ metastatic melanoma as requested for co-dependent reimbursement process in Australia

Research question in Final Decision Analytic Protocol:

Is BRAF genetic testing for V600E or V600K mutations in tumor samples of patients with resectable stage IIIB, IIIC or unresectable stage IIIA, IIIB, IIIC or stage IV cutaneous melanoma, in addition to usual care or targeted treatment with vemurafenib in patients with unresectable stage IIIC or metastatic stage IV cutaneous melanoma, safe, effective and cost-effective compared to usual care alone without BRAF testing?

12 scenarios requested in total, based on:

- Definition of V600 mutation:
  - All V600, V600E and K, V600E
- Stage of disease:
  - Unresectable stage IIIC or stage IV (trial-based)
  - Resectable stage IIIB, IIIC or unresectable stage IIIA, IIIB, IIIC or stage IV
  - Resectable or unresectable stage IIIA, IIIB, IIIC or stage IV
  - Unresectable stage IIIA, IIIB, IIIC or stage IV

Co-dependent reimbursement submissions offer additional challenges

- Determining the ‘gold standard’ test
- Does the diagnostic test used in the clinical studies match country practice?
- Comparative accuracy data comparing evidentiary standard against commonly used tests (e.g. in-house IVDs)
- Complexity involved with accommodating multiple testing scenarios requested
- Establishing the cost of the service
  - Not easily defined (as with drug) and must involve relevant practitioners
- RCTs of the drug and test cannot answer all of the questions asked
  - Data for subgroups
  - Data in wildtype patients

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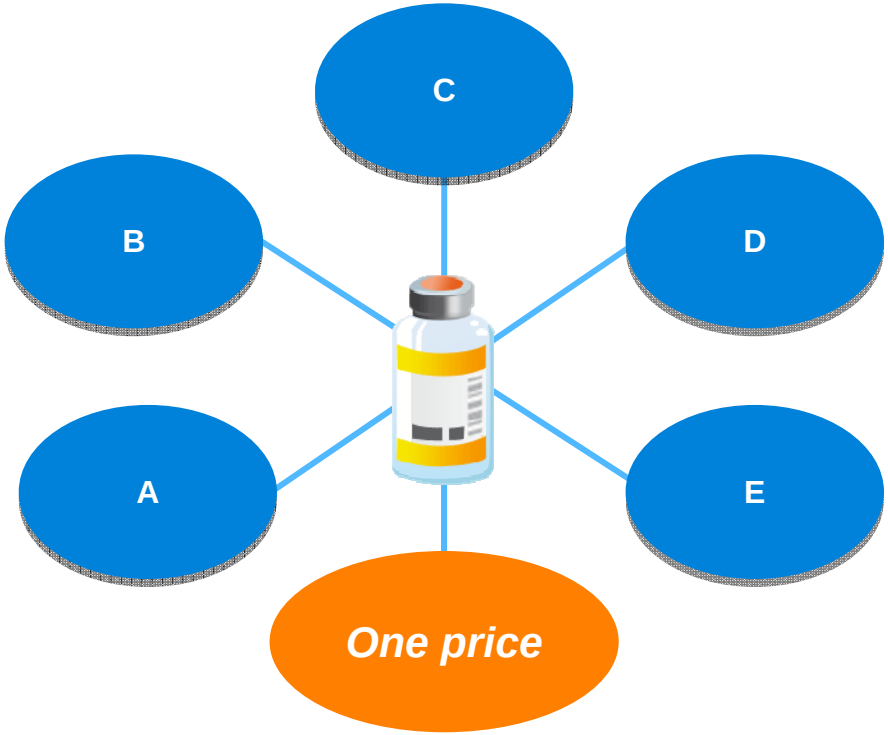
Personalised Healthcare will require a new personalized reimbursement model based on value

- The prices for our medicines reflect the value that the innovation delivers to patients, providers, and societies
- The value of our medicines in a personalized healthcare setting varies across different disease segments
- If prices are based on value, then they should vary in line with disease segments

Why personalized reimbursement model?



For illustrative purposes only

- Drug X is indicated for 5 diseases/disease segments
- Clinical benefit derived from drug X varies by indication
- Regardless of potential clinical benefit, the price of the medicine remains the same
- If price is set in line with the higher value indication, there can be issues around reimbursing patients in indication with perceived lower value
- Conversely Manufacturer will not be rewarded for the innovation if price is set at the lower value indication

A personalized reimbursement model would allow differences in potential clinical benefit to be realized through pricing according to the value a medicine delivers for each specific disease indication

Implementing personalized reimbursement models will require an appropriate IT and financial infrastructure

- Medicine will be sold at a nominal price
- Different reimbursement arrangements (eg patient access schemes, cost caps, discounts) will be defined by disease segment and treatment combination
- Timely information on actual utilization of the medicine will be collected
- Financial reconciliation based on utilization data

Example UK: Systemic Anti Cancer Therapy Dataset can facilitate personalized reimbursement models

- Defined dataset to be reported by all cancer treatment centers for all patients treated within the NHS
- Initial 8 data fields sufficient for personalized reimbursement models
- Data will be submitted and aggregated by NHS
- Personalized reimbursement model is a special form of patient access scheme

Why can’t we make it simple and rather continue to work with an “average price”

- Value assessment (national and provincial level) is conducted by disease segment
- Providers and local payers have become price sensitive:
  - Will be happy to use medicine in “high value segment” where value is above the average price
  - Will not support utilization in lower value segments, where other treatment alternatives are deemed more cost-effective
- Patient access to innovative targeted therapies will be limited or delayed

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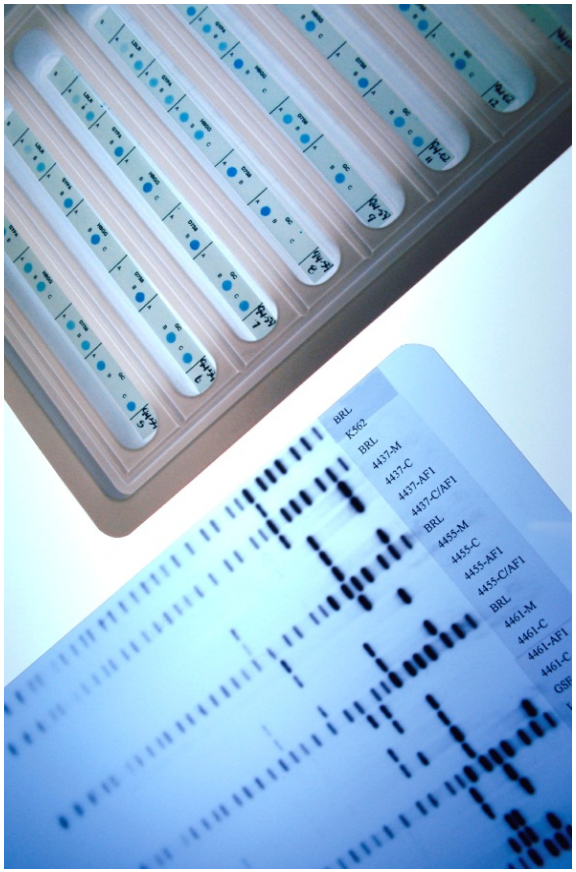
Conclusions: personalized healthcare is aligned with HTA but requires a new personalized reimbursement model



- PHC promotes a differentiated assessment of the incremental patient benefit
- HTA and value based pricing are aligned with PHC
- PHC requires personalized reimbursement models to align value and price
- This will ensure patient access while providing rewards for industry
- Practical implementation requires a basic registry infrastructure like SACT

Doing now what patients need next