Generating and leveraging RWE to drive pricing & access

The importance of Multiple Data Source Integration and Value Attribution in Multi-Component Disease Management

An Ipsos Point of View (POV)

World Evidence Pricing and Access Congress 2022

Acknowledgements

It is important to bring together different perspectives in order to address future challenges

This POV draws on the views of:

- Ipsos Market Access Teams in EU, US, and APAC
- Ipsos Digital and Connected Health Centre of Expertise
- Ipsos Multi-Source Data strategists
- Ipsos Syndicated Real World Evidence Services

Contents

01

Evolution

Healthcare is evolving rapidly

ISPOR has published[1] its Top 10 Trends 2022-23…

1. **Real-World Evidence:** Using RWE in Healthcare Decision Making
2. **Value Assessment:** Informing Value-Driven Healthcare Decisions
3. **Health Equity:** Addressing Disparities in Healthcare
4. **Healthcare Financing:** Funding Innovative Health Technologies
5. **Patient Engagement:** Infusing the "Patient Voice" in Healthcare Research
6. **Drug and Healthcare Pricing:** Improving Price Transparency
7. **Public Health:** Focusing on Key Priorities
8. **Health Technology Assessment:** Supporting Cross-Country HTA Cooperation
9. **Health Data:** Addressing Infrastructure and Interoperability
10. **Artificial Intelligence:** Leveraging AI and Advanced Analytics

These will have profound consequences for:

Evidence use

Value measurement

Pricing Assessment

1 https://www.ispor.org/heor-resources/good-practices/article/ispor-2022-2023-top-10-heor-trends

In the future, value will increasingly be delivered by multi-component disease management rather than by drugs (or interventions) in isolation

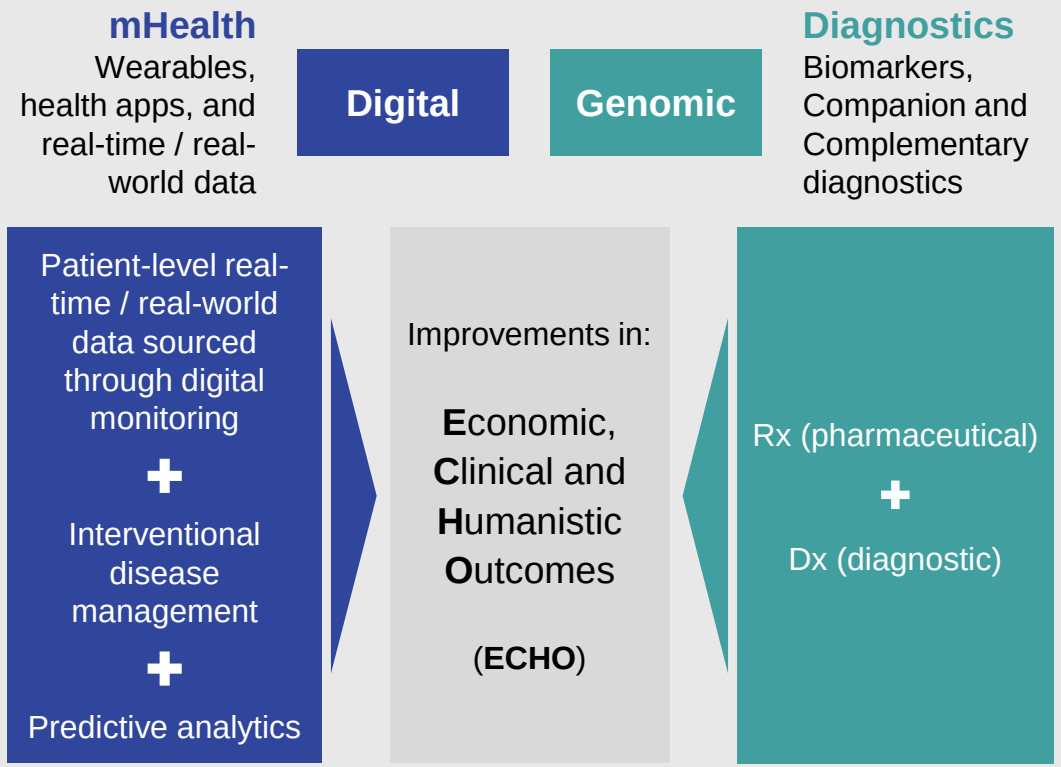
The gradual evolution and fusion of:

- **Biomarker informed disease management:**
  - Genomics/Proteomics
- **Real-time informed disease management:**
  - Digital/Wearable technologies
- **Intelligent smart disease management:**
  - Advanced analytics, software, algorithms, and artificial intelligence

is opening up opportunities to enhance the efficiency and effectiveness of healthcare delivery by making treatment more personalized and precise.

This will create challenges for value, price, access and health technology assessment; and will require new approaches to value evidence generation that will involve innovative multi-source data integration[1].

The convergence of digital and genomic technologies to enhance the efficiency of healthcare delivery and make disease management more personalized and precise[2]



1: Pharmaceutical Management Science Association. The challenges of optimizing health outcomes, pricing and market access in a digital world where Personalized Data and Big Data collide. Teale et al 2018

[2] Adapted from: Bhavnani, Sanjeev P.; Narula, Jagat; Sengupta, Partho P. (7 May 2016). "Mobile technology and the digitization of healthcare". European Heart Journal. 37 (18): 1428–38.

The transition to multi-component disease management will not be smooth

- Systemic and stakeholder barriers will need to be removed
- Incentives will need to be created
- Collaboration will be required between stakeholders
- Data from multiple sources will need to be integrated
- Healthcare IT systems will need to be modified

Barriers to delivering the promise of digital and genomic technologies[1]

Systemic Barriers	Stakeholder Barriers
Regulatory systems	Payer & patient willingness to pay
Health Technology Assessment (HTA) systems	Physician & patient willingness to use
Coding, payment, and funding systems	New roles of patient, physician & data in disease management

- Without a **clear path to monetization**, investment will wither.
- Current Payment systems reflect the **episodic nature of healthcare** (i.e. payment tied to event or “encounter”).
- There are no (financial) incentives to use transmitted data. For technologies operating outside “encounters” a **lack of reimbursement mechanism** for User or manufacturer is a significant barrier to uptake.
- Digital Health generates data that is **not (yet) coordinated or integrated with** Physician decision-making and disease management.

[1] ISPOR Poster 2019: “What actions should be taken now to facilitate market access and value being delivered in the future” - Teale, Morrison. Klebba

The approach to pricing and access will need to be re-engineered to address 4 factors

Evolution

Science and Technology

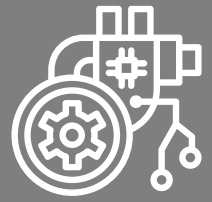
The biggest disruptor to the healthcare landscape of the future.

Multi-Component Disease Management

The linking of patient-level, real-world/real-time data – together with biomarker informed precision medicine / personalized healthcare.

Multi-Stakeholder Value Attribution

A shift in focus from the assessment of a drug or device in isolation to a more holistic assessment of the value of healthcare – disease prevention and disease management.



Multi-Source Data Integration

Regulatory and Health Technology Assessments increasingly embracing data and evidence beyond traditional randomized controlled trials.

Current approaches to the assessment of price fail to address the dynamic nature of multi-component disease management

Pricing Method	Cost-Plus Pricing	Competitor-Pricing	Value-based Pricing
Definition	Pricing based on cost of manufacturing the product plus a specified margin	Pricing based on how competitors price their products (discount or premium to competition)	Pricing based on the perceived value to the customer
Weaknesses	• Sub-optimal pricing decisions • Easily leads to profit loss from either not satisfying high demand or underutilization of capacity	• May lead to price wars • Risk of cannibalization • “Undervaluation" of innovative products and services.	• Requires evidence of value • Difficult / costly to measure

Future approaches may need to consider value attribution and give greater weight to the type, availability and timing of evidence[1]

[1] Ipsos webinar: The future of Pharmaceutical Pricing May 2021

02

Value

Value attribution will become important in the future

Consider two situations where this is may be the case:

1

Pricing of combination therapies and “stacks”

2

Access/Funding negotiations spread across multiple manufacturers and technologies

- Challenges of precision medicine (genomics) and digital health (apps, wearables, machine learning and artificial intelligence)
  - Different funding flows
  - Different assessment systems

The pricing of combination therapies and “stacks”

Multi-Product Regimen

A combination regimen comprises two or more constituent medicines that companies are expecting to be priced to value. Payers are often not willing to pay more per health unit gained for multi-product (combination) regimens than for single product regimens. Standard health economics methods are agnostic to the composition of costs.

Multiple Owners

If all constituents are owned by two or more different companies:

- They are prohibited by competition law to negotiate with each other on the prices of individual constituents that comprise the regimen, and propose an agreed total treatment cost.

One Owner

If all constituents are owned by a single company:

- That company will be able to present a total cost of regimen that is satisfactory to the payer and price the constituent medicines accordingly

How should value and revenues be allocated between the companies?

What are the implications for other indications of the constituent medicines?

To develop implementable solutions at least 4 problems will need to be solved[1]

Value

1 The Incentive Problem

As the value of a medicine may differ by use (monotherapy vs combination use; first line vs subsequent line, tumour type or indication etc), this difference in value will need to be reflected in the reimbursed price.

Should an assessment of the value of a medicine within a combination regimen result in a price adjustment to a medicine already reimbursed in another use, there will be a strong disincentive for the owner of this medicine to renegotiate should that adjusted price flow on to all reimbursed uses of that medicine.

2 The Value Attribution Problem

How should the value of the combination be apportioned between the constituent medicines of a regimen, and therefore how should the individual medicines be priced to reflect that value assuming a given willingness to pay for regimen itself?

3 The Competition Law Problem

Within the limits of existing competition and anti-trust law, how can competitor companies arrive at “agreed” prices for the constituent medicines within a regimen, so that the total cost of the latter is commensurate with the value of the treatment?

4 The Implementation Problem

Even if all such problems are solved, they need to be implemented within a given pricing and reimbursement system and its laws and policies.

In order to solve the implementation problem, it is likely that a form of indication or multiuse pricing will be required. This is often viewed as complex, requiring separate prices for each indication or use but pragmatic approaches utilising weighted-average prices can be adopted (e.g. In France and Australia).

[1] *Outcomes-based Value Attribution Framework for cancer combination therapies OHE 2021*

The problem becomes even more challenging when co-dependent value is spread across multiple manufacturers and technologies[1]

Value

Manufacturer 1

Remote real-time monitoring

Manufacturer 2

Diagnostic for biomarker detection

Manufacturer 3

Drug 1 of combination (“stack”)

Manufacturer 4

Drug 2 of combination (“stack”)

Manufacturer 5 Software, Apps, Algorithms, AI, Machine Learning, Predictive Analytics

Potential Solutions

- A DRG for a disease, which encompasses all of these pieces together, giving a more holistic view of cost and outcome?
- Price everything separately, but how do you then take that forward and price according to value of overall health gain which is dependent on other parts of the treatment process?

[1] *ISPOR Poster 2021: The Monitor Intervene Predict Value Framework – Teale, Glover, Hoad*

03

Evidence

An abundance of data

E.g. Multi-source data including RWE (providing either validating or conflicting insights)

A shortage of evidence

E.g. Single arm open label studies, Tumour agnostic licensure leading to pricing in indications where there is no data

There are a lot of useful data available in addition to RCTs

Examples include:

- Real-time data: Data collected through digital health technologies, including apps and wearables;
- Primary care databases;
- Secondary care databases, e.g. Hospital Episode Statistics (HES);
- Syndicated data captured by market research;
- Audits of clinical practice, and registries of the use of medicines, devices and other technologies;
- Surveillance and monitoring data, e.g. drug safety monitoring data;
- Datasets released by public health and social care authorities;
- Data that represents the views and experiences of people using services, whether captured formally, e.g. via surveys or informally, e.g. via online discussion forums and social media or patient experience sites such as healthtalk.org;
- Data collected by patient organisations;
- Social Media data

3 key conditions must be met for their use in price negotiation.

The data must be:

- ✓ **Available**
- ✓ **Accessible**
- ✓ **Acceptable**

HTA is accepting a broader range of data sources

Evidence

Pre-Launch

- Standard of Care
- Financial Impact
- Burden of Illness
- Unmet Needs
- Patient Impact / Patient-Relevant Outcomes

REAL WORLD EVIDENCE

Helps us understand…

Post-Launch

- Usage
- Clinical Effectiveness
- Safety
- Budget impact
- Cost Effectiveness
- Patient Preference

HTA is accepting a broader range of data sources

Evidence

Pre-Launch

REAL WORLD EVIDENCE

Post-Launch

Helps us understand…

Country (Agency)	Changes to evidence acceptance (2021 onwards)
UK (NICE)	NICE plans to use broader range of data and analytics including patient registries, audits of clinical practice, primary and secondary care databases, and genomic data
France (HAS)	Comparison of reimbursement decisions before and after RWE review in France. When assessing new medicines for reimbursement decisions if there is an uncertainty about the generalisability of RCT data to real-life practice, the Haute Autorité de Santé (HAS) may request the collection of real-life data in the form of real-life post-registration studies to be conducted by the pharmaceutical company.
Germany (IQWiG)	IQWiG says data from registries are appropriate for use in assessments. in some cases (for example orphan drugs), data may be lacking at the time of market access to fully assess the benefit of a product. These evidence gaps can be filled by observing the use and effect of the drug in clinical practice
USA (ICER)	ICER's updated assessment process leverages observational RWE analyzed by Aetion, as part of the ongoing collaboration between the two organizations, and consistent with ICER's commitment to expand use of RWE to complement other sources of information used in its value assessments. Aetion researchers use Optum's de-identified Clinformatics® Data Mart, Commercial and Medicare Advantage claims database, to generate the RWE.

Sometimes RCTs are not available or appropriate, pushing us to need alternative sources of evidence

Non-comparative data, plus modelling, may be acceptable[1].

RCTs are not always ethical, feasible, or practical

A placebo/comparator is likely to be less effective than the evaluated intervention under evaluation (e.g. immediately life-threatening disorders).

Detecting statistically significant differences between treatment arms will be hard due to low n-numbers (e.g. rare genetic disorders).

There are no established comparator treatments (e.g. some advanced cancers).

Uncontrolled studies are acceptable

Where change in a condition can clearly be attributable to the therapy, placebo response is minimal, prognosis bleak, and there is no acceptable control arm (FDA (2007)).

The background disease and its natural history is important – elapsing/remitting diseases would be inappropriate, as are time-to-event endpoints.

The endpoint must also be "hard/objective".

Noncomparative studies may provide the "best available" evidence

Noncomparative studies may provide the "best available" evidence to inform health care decision making:

- In the clinical trial setting: e.g. dose-ranging studies, single-arm trials, case series, and case reports.
- In the "real-world" setting: registry studies, claims data, and some observational designs.

Modelling

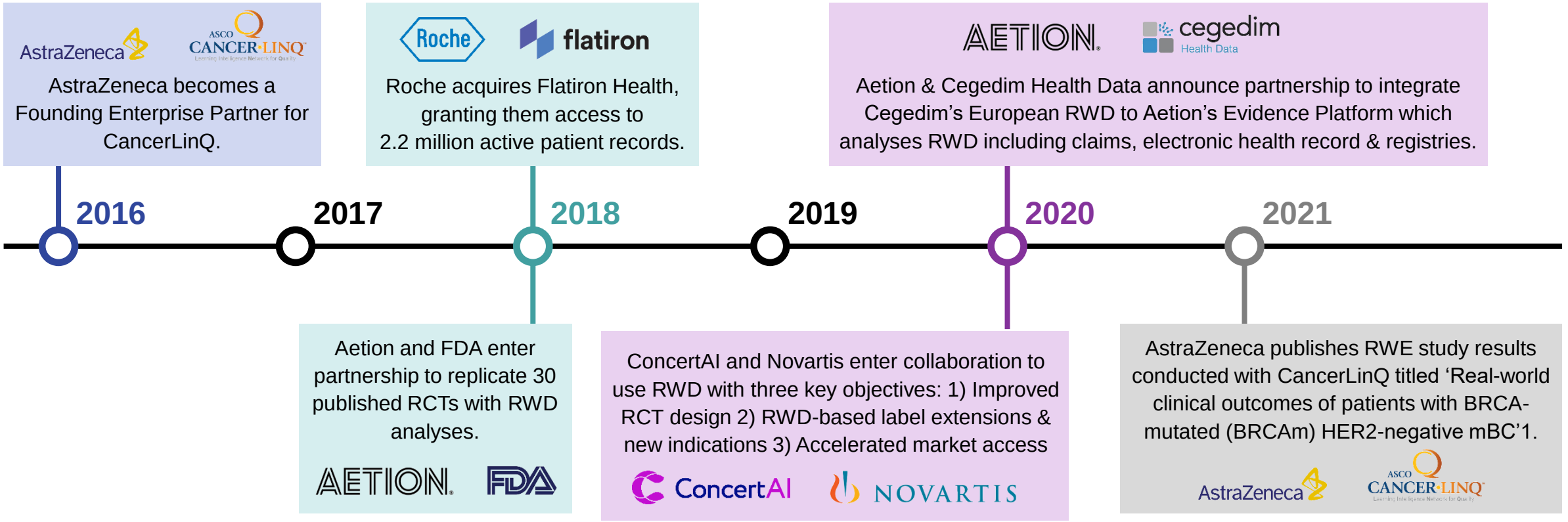
Comparison of single-arm trial with an artificial comparator arm built out of real-world data, based on modelling, has been used in regulatory submissions (FDA/EMA) and health technology assessments.

[1] *EPA Congress 2021: Pricing & Access Challenges in the absence of data. Teale et al.*

Strategic partnerships between manufacturers and data providers are increasingly needed to access data

Evidence

Manufacturers and assessors have entered long-term agreements with RWD providers to increase access to data



With the establishment of these relationships, manufacturers can readily access RWD which they can utilise across their portfolios. RWE will increasingly become a differentiating factor in pricing submissions.

Single source data may not be sufficient. Multiple data source integration may be required.

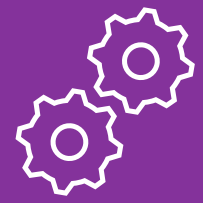
Evidence

Market insight

- Proprietary syndicated data
- Data analytics with traditional market research
- Behavioural science
- Creative labs
- Social Intelligence Analytics (SIA)

Third Party External Sources

- Prescription data
- Electronic medical records (EMRs)
- Health resource utilization (HRU)
- Claims data
- Real-time / wearable data
- Social media data



Manufacturer's Internal Data

- Customer relationship data (CRM)
- Internal resource allocation

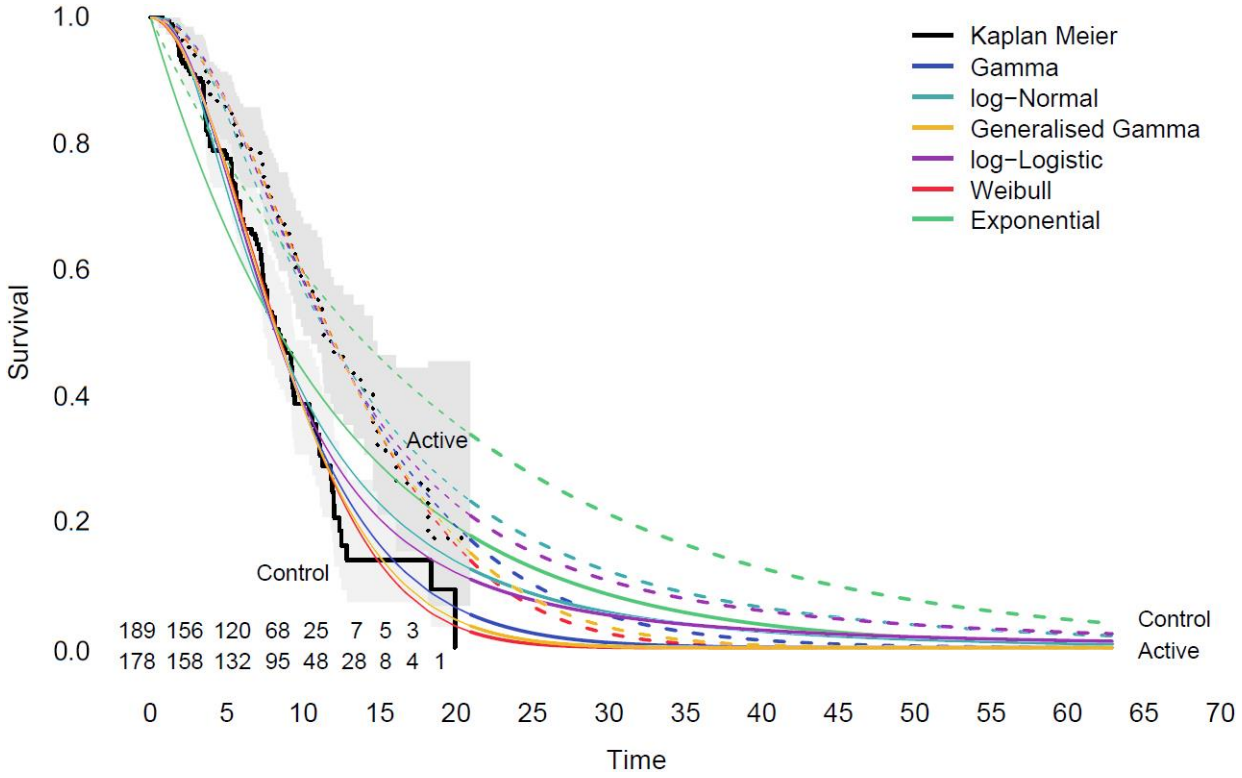
Ref: Ipsos Multi Source Data Strategy - internal presentation

Integration of data from multiple sources often needs to complemented by modelling and data engineering[1]

Linking RCT with Real-World Evidence (RWE) will help answer payers' treatment sequencing questions.

Curve fitting and data extrapolation are common but sometimes, due to cross-over, modelling overall survival cannot be demonstrated using classical biostatistics. Solutions from HTA include use of more sophisticated methods such as inverse probability of censoring weighting (IPCW) and Rank-Preserving Structural Failure Time (RPSFT).

Quality adjusting data (e.g. PFS) can sometimes magnify a small difference between products into one that has significant value differentiation in patient, physician, and payer eyes.



[1] *Ipsos Secondary Research plus: ISPOR Health Science Policy Council. "2022-2023 Top 10 HEOR Trends". An ISPOR White Paper. January 2022.*

Systemic changes may be necessary to make multi-source data integration feasible

Partnering with health systems may offer the following advantages:

- A well-established buy-and-bill infrastructure;
- Centralised prescribing influence;
- Centralised electronic health records to facilitate the identification of patients suitable for Leqvio;
- Established processes for the adoption of new medicines.

Compliance with the reimbursement conditions will be verified by a monitoring committee in each autonomous community, which will be established by the regional health administrations and Novartis.

The results will be communicated to the DGCYF (Directorate General for the Common Portfolio of NHS Services and Pharmacy) to ascertain whether the price needs to be reviewed. The VALTERMED online platform will be used to track compliance with the DGCYF's pharmaco-clinical protocol.

If sales exceed forecasts, Zolgensma's price will be reduced. Expenditure will be tracked by means of SEGUIMED—a computer application that manages data related to drug transactions between manufacturers, wholesalers and pharmacies

Ref: LinkedIn - Future of Market Access – Grubert et al - Feb 2022

04

Conclusion

Questions that can be addressed using multi- source data integration

1.

Treatment Sequencing

The payer value story and messaging should not be just restricted to a particular position/line in therapy.

Payers, physicians, and patients are interested in the outcomes (clinical, economic, and humanistic) of the management of disease from diagnosis to death (or cure).

Questions that can be addressed using multi- source data integration

1.

Treatment sequencing

2.

Affordability

Companies can more easily move on from the simple concept that a product (the pill) has a price ($X/month).

Companies are increasingly offering:

- Innovative product propositions– eg. drug/administration / diagnostic / digital app solution packages
- Outcomes-based managed entry agreements
- Innovative pricing propositions – single lifetime pricing, annuities etc
- Financial engineering through the apportionment of value

Questions that can be addressed using multi- source data integration

Conclusion

1. Treatment sequencing

2. Affordability

3. Predictability

- Payers value both clinical and economic predictability - in some cases more than cost-effectiveness
- Clinical predictability is driven by patient and treatment selection, increasingly informed by genomics and biomarkers
- Economic predictability can often be managed by the structure of the pricing proposition and financial engineering

Questions that can be addressed using multi- source data integration

1. Treatment sequencing

2. Affordability

3. Predictability

4. Outcome driven decision-making

- Endpoints & Outcomes spread across multiple data sources
- Classical clinical outcomes based on RCTs (such as median OS in Oncology) are preferred by physicians
- Patient relevant outcomes (multi-sourced) increasingly valued
- Payers increasingly faced with an array of outcome metrics some more relevant than others to their KPIs
- Endpoint metrics that are predictive of outcome resonate strongly with payers

To build a case for funding and access as healthcare evolves towards multi-component disease management

Future approaches to the assessment of price may need to consider value attribution and give greater weight to the availability and timing of evidence

There will be a **need to adapt HTA processes** to address assessment challenges for clinical uncertainty and affordability. **Innovative source data and financial engineering** are promising solutions to overcome those barriers.

The **availability of additional data from multiple sources** (e.g. claims data, digital health technologies, electronic medical records, Tx and Rx data) can help reduce this uncertainty.

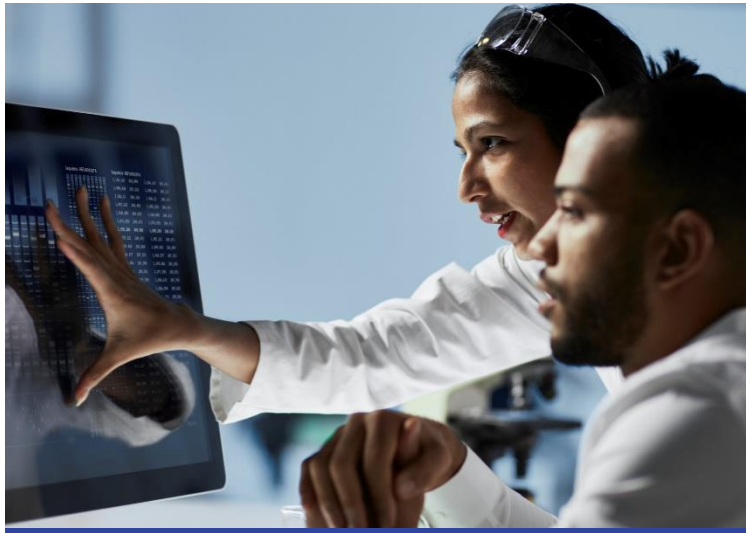
The breadth of RWE acceptable to HTA has increased significantly and presents a major opportunity for manufacturers to demonstrate the value of their products.

Non-comparative studies, uncontrolled studies, disease & drug registries, and other sources of real-time real-world evidence (RTRWE) increasingly will **be used to inform healthcare decision making**

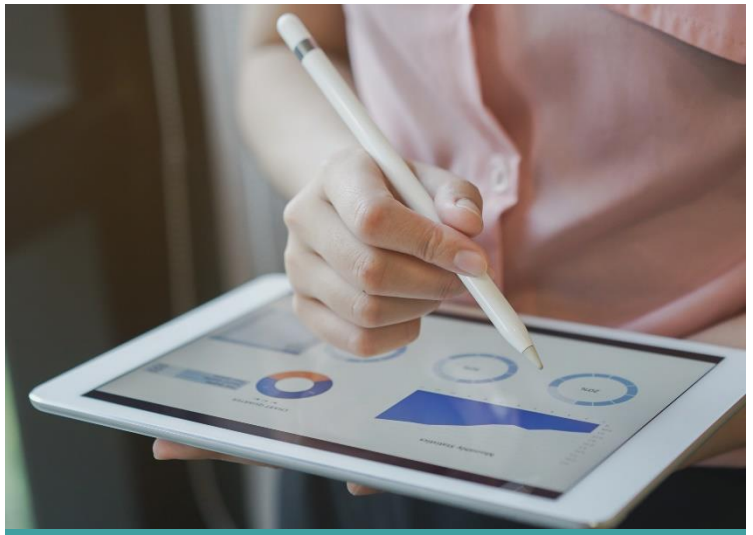
Data engineering will be necessary to integrate the data from multiple sources, this will require pre-planning, methodological rigour and validation, and sometimes systemic changes

Adapted from: ISPOR Poster 2021: Leveraging RWE and integrating multi-source data to build the case for funding and access for rare disease drugs - Roldan-Gomendio et al

In summary



- Value will be delivered by multi-component disease management rather than by drugs (or interventions) in isolation.



- More and more alternative, often unstructured, data sources will be available and acceptable to use.
- However collaboration and systemic changes may be required to access this

- Multiple Data Source Integration will be required to demonstrate value
- Value attribution may also be required to ensure fair returns to all stakeholders.

THANK YOU.

Chris Teale

Senior Vice President Market Access
chris.teale@ipsos.com

Ipsos is a global insight, analytics and advisory partner to the healthcare sector.
Our multi-disciplinary teams deliver integrated services and proprietary real-world evidence across the product lifecycle

Chris Teale

Senior Vice President Market Access
chris.teale@ipsos.com

Chris Teale brings extensive practical and academic experience, across both Marketing and R&D, from a 30-year career within the pharmaceutical industry, having held a number of leadership positions at both Global and European level at AstraZeneca, Allergan, Novartis and Fisons.

Within Ipsos Market Access, Chris leads the European Oncology and Personalised Healthcare (PHC) Practices and is also Lead on Global Biosimilar Strategy and War Gaming / Competitive Simulation. His specialist areas of focus are policy influence in Autoimmune Diseases and Oncology; and innovative approaches to pricing and market access.

Chris gained a BSc degree in Mathematics from Newcastle University, and also studied at Loughborough University and INSEAD Business School. He is an occasional lecturer on health economics and pricing and reimbursement at Kings College London and University of California (San Diego).