30 Major Future Challenges in Evidence, Pricing & Access and How to Overcome Them

May 2023

Executive summary

Much has been written about the current trends in healthcare, often punctuated with buzzwords, including: Real World Evidence (RWE), health data, patient engagement, health equity, advanced analytics and, more recently, artificial intelligence.

However, less has been written about the consequences of these trends for health outcomes, or the challenges that may arise from them in terms of the affordability and sustainability of healthcare systems, and the growth and profitability of the healthcare industry (pharma, biotech, medical technology, hardware and software).

Based on research we recently presented at the World Evidence, Pricing & Access Congress, we have identified 30 major challenges that will need to be overcome if, in a healthcare world that is evolving rapidly, real world outcomes are to meet the theoretical promises.

Along the way we propose solutions (approaches that companies and healthcare systems need to consider), identify key facilitators, and finally conclude that the status quo is not an option.

Success will require significant systemic, stakeholder and organisational change.

01

BACKGROUND & METHODOLOGY

Healthcare is evolving rapidly

Last year, ISPOR published 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

To explore the consequences of these, Ipsos posed two questions:

- What challenges will these bring between 2023-2030?
- How can these challenges be overcome?

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

Expert opinion was sought using a 2-Cycle Delphi approach with internal and external input

Delphi Cycle 1:

- Generation of a list of the key challenges:
  - Evidence
  - Pricing
  - Access
- over the period 2023-30 in oncology and immunology.
- No limits on numbers of challenges

Delphi Cycle 2:

- Results of Cycle 1 shared amongst participants
- Participants confirm or amend their input
- Challenges clustered
- Barriers identified
- Solutions identified

Internal:

- Ipsos Market Access Teams in EU, US, and APAC
- Ipsos Oncology Centre of Expertise
- Ipsos Autoimmune Centre of Expertise
- Ipsos Global Oncology Monitor (Syndicated Real World Evidence)
- Ipsos Autoimmune Therapy Monitors (Syndicated Real World Evidence)
- Ipsos Molecular Diagnostics Monitor (Syndicated Real World Evidence)
- Ipsos Trends and Foresight

External:

- Payer experts in immunology and oncology via 2 roundtables undertaken for clients

Participants: Internal: n=35 External: n=6

The scope included:

The Complete Lifecycle Pathway

- From drug discovery to loss of exclusivity (LoE)

The Digital Contribution

- Digital health technologies based on monitoring, intervention, predictive analytics, and AI

The Genomic Contribution

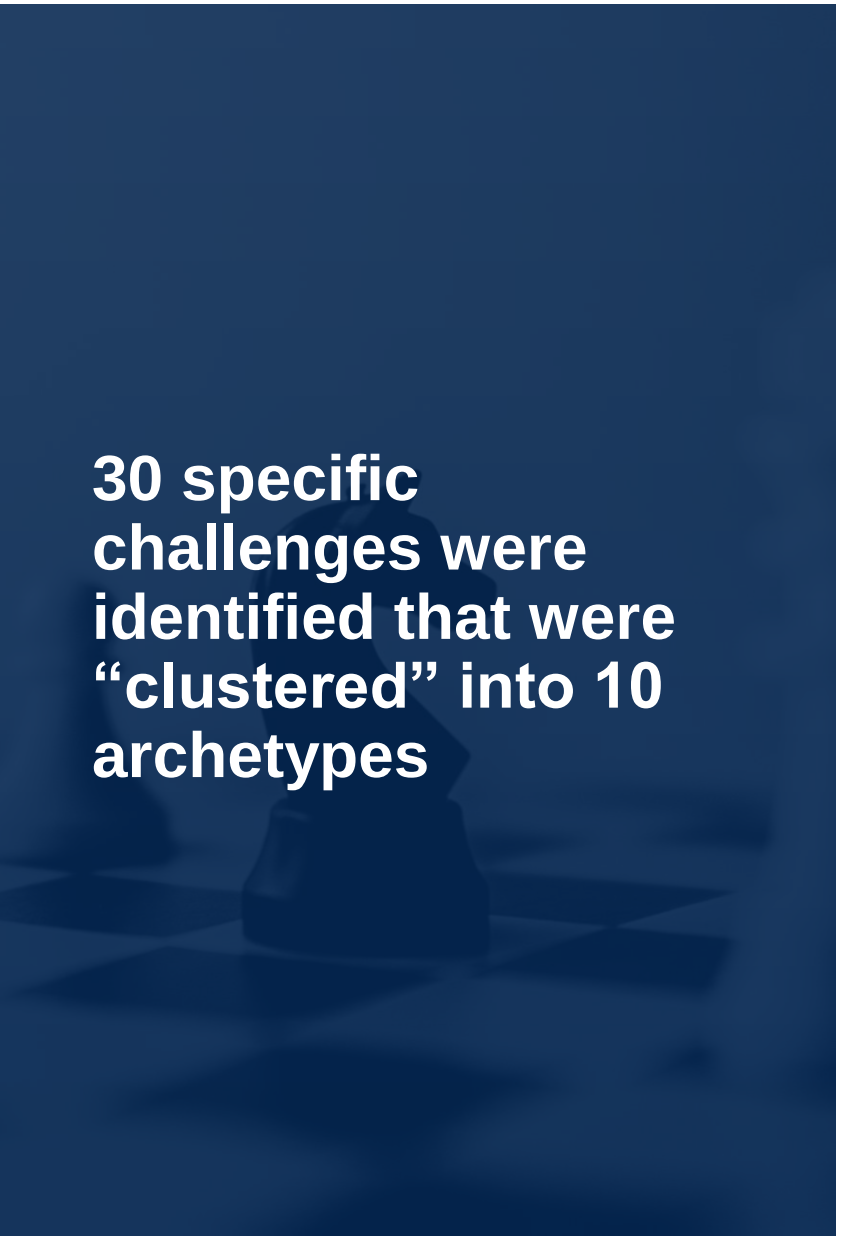
- **Patient Selection** informed by genomics and molecular diagnostics
- **Assessment of Co-dependent Value (Rx-Dx)** where biomarkers have a role

Consideration of Value Attribution

- Where value is delivered by multi-component disease management rather than by drugs or interventions in isolation

02

CHALLENGES



30 specific challenges were identified that were “clustered” into 10 archetypes

1	Affordability
2	Evidence
3	Assessment
4	Pricing
5	Differentiation
6	Sequencing
7	Personalisation
8	Value Attribution
9	Portfolio Optimisation
10	Pace of Change

Affordability

1

Need For Alternative Funding Models

Innovative managed entry agreements such as risk sharing, subscription models, and solutions from financial services industry will be required. To be acceptable they will need to be easily verifiable and carry minimal administrative overhead.

2

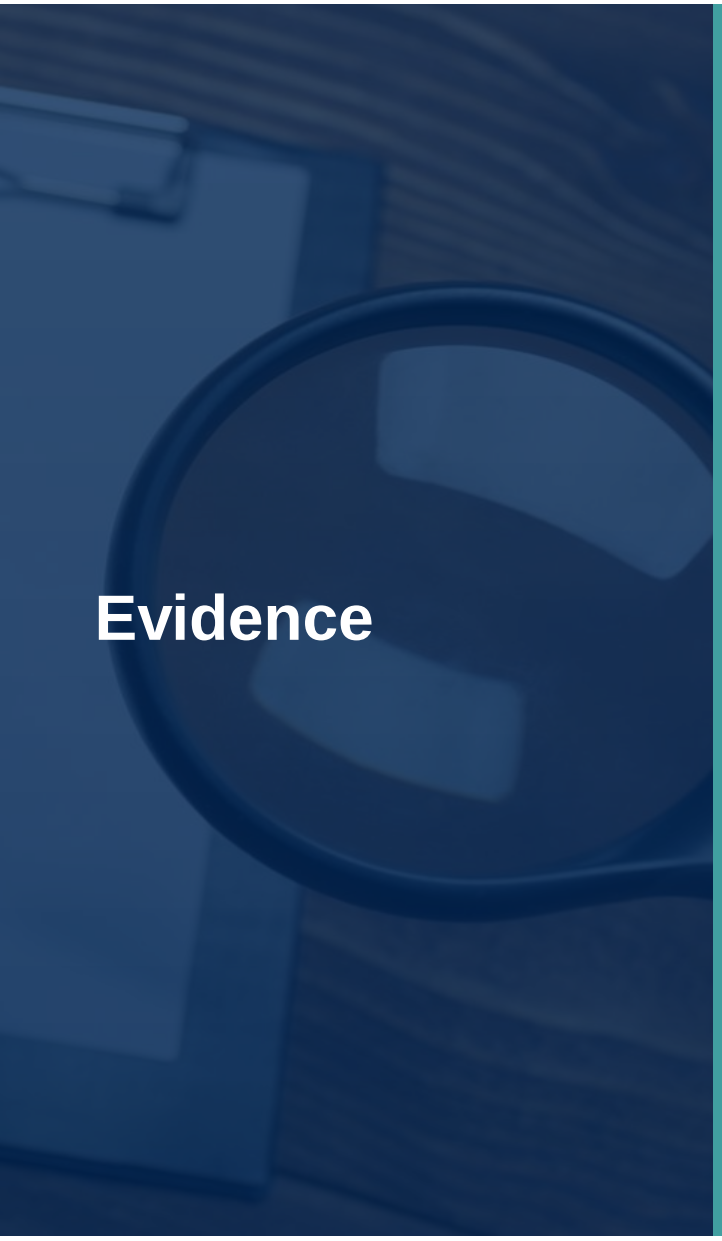
Equitable Affordability

Solutions will be required that address affordability differences between countries, e.g., **Equity Based Tiered Pricing (EBTP)** based on gross national income (GNI) per capita adjusted for purchasing power parity.

3

Funding ATMPs In Large Populations

Reimbursement of ATMPs (cell and gene therapies) where there is a very high upfront cost, often single payment, is challenging. To date, this challenge has been in rare diseases. The challenge will become much greater as ATMPs move into common diseases with large populations.



Evidence

4

Availability, Accessibility & Acceptability of Evidence

RWE, digital health technology data, advanced analytics, and modelling in Payer/HTA assessment have the potential to add value, but to be utilized these additional data sources need to be Available, Accessible, and Acceptable. Often a significant limitation.

5

Integration of Multi-Source Data

Using additional data sources can bring added value, but building a robust value story by integrating an **abundance of sometimes conflicting and contradictory data** may bring challenges around validity, relevance, reliability, and reproducibility.

6

Tumour Agnostic and Rare Disease Licensing

With developments in biomarker understanding leading to tumour agnostic licensure, plus the ethical and logistical challenges of RCTs in rare diseases, building a robust and compelling value story for Payers/HTA in the **absence of data** will be a significant market access hurdle.

7

Divergence of Regulatory and Payer Evidence Requirements

In the future, healthcare will be delivered increasingly through multi-component disease management rather than by drugs or interventions in isolation. This will lead to a widening gap between regulatory and payer evidence requirements.

8

Ethical and Legal Issues: Data Ownership, Use and Abuse

Ethical and legal challenges over ownership and use and abuse of data will increase. Significant regulatory challenges will emerge from interventions that are driven by automated analytic algorithms/machine learning/artificial intelligence.

Assessment

9

Convergence of Regulatory and Payer/HTA Assessment

Closer integration of regulatory and HTA with common clinical assessment, EU HTA harmonization, DARWIN EU RWE coordination are planned. This evolution will face the challenge of differences in clinical practice and healthcare funding systems across the EU.

10

Integration of elements of “Ignored Value” Into HTA Assessment

Many elements of value are excluded from HTA assessments: Cost savings outside the health system, reduction in uncertainty, value of hope, real option value, insurance value, and scientific spill-overs. Integration will evolve driven by the shifts towards integrated care.

11

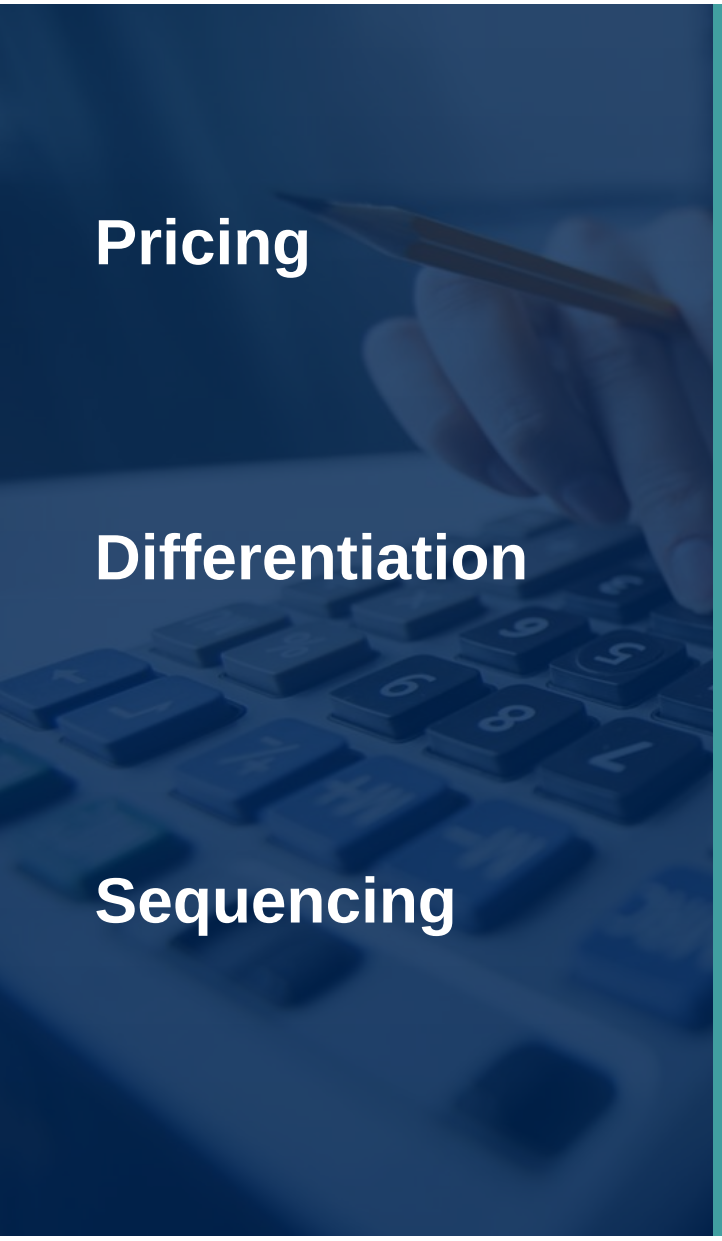
Linking Endpoints and Outcomes

Cost and value are driven by real world outcomes however clinical trial endpoints are not always predictive of outcomes. Extrapolation from endpoints to CV and organ failure risk reduction, and outcomes associated with disease modification, will be addressed by conditional reimbursement, coverage with evidence development, and dynamic pricing models.

12

Unmet Need and Burden Of Illness

There is a widening perception gap between unmet need and burden of illness. Payers often perceive there is little unmet need and have a low willingness to pay (WTP). Manufacturers believe there is high unmet need and have high expectations for both price and volume.



Pricing

Differentiation

Sequencing

13

Price Contagion

Many major products are approaching loss of exclusivity (LoE) resulting in significant price reduction. New products will increasingly face challenges in establishing a value-based list price and even greater challenges in maintaining net price due to price contagion.

14

Price Modification

The increased use of therapy stacks of high value / high price products will bring affordability challenges. Manufacturers will face price reductions in all elements of the stack.

15

Establishing Differentiation When Products Are The Same Or Similar

Differentiation will be critical for commercial success post patent expiry for originators, generics and biosimilars of blockbuster products. Establishing innovative Product, Price, Proof, and Performance propositions will be critical for success.

16

Drug Delivery Differentiation

Drug delivery will be a key differentiator of new products and a potential defense strategy for products facing LoE. Understanding the trade-off of duration of effect, patient preference, convenience, compliance and clinical / economic real-world outcomes will be key for success.

17

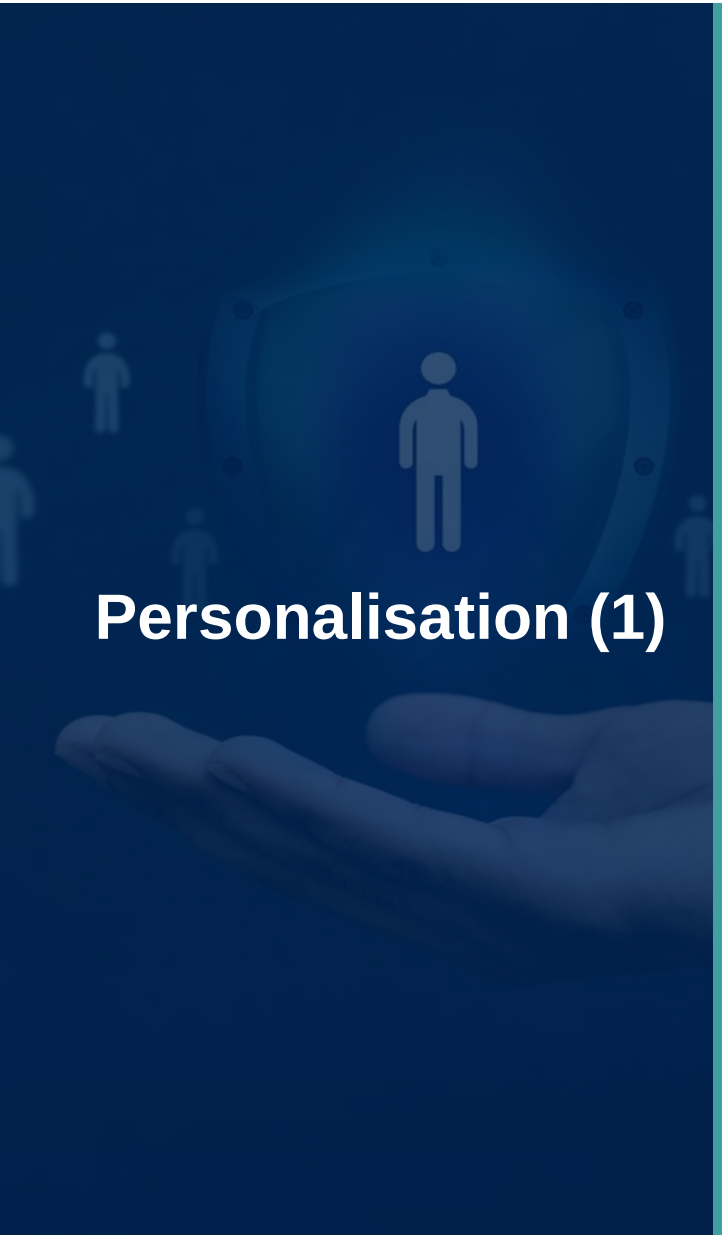
Treatment Order Sequencing

Measuring the value of a treatment sequence rather than in a single line of therapy. Pricing to the end-goal: A therapy is launched in late line, but the goal is 1st line. How to price in a way that may dilute initial revenues but, under uncertainty, eventually maximises lifecycle revenues.

18

Early Detection And Diagnosis

Early screening initiatives for under-diagnosed diseases (e.g. NASH) face challenges in the real world, for payers (unbudgeted costs) and policy makers (around the benefit threshold) and for patients and physicians (when there are no treatments accessible / available).



Personalisation (1)

19

Patient expectations

The increasing role of the patient: knowledge, expectations, increased involvement in decision-making but NOT correlated with patient willingness to pay. Advancement of freely available information through the internet and web-based bots e.g., Google, ChatGPT

20

Making Digital Healthcare Smarter

Payers will be unwilling to reimburse digital health technologies without evidence of improved outcomes. Behavioral change alone will be insufficient. Making digital healthcare smarter by integrating monitoring, intervention and prediction into disease management will be key

21

Molecular Diagnostics-Informed Drug Commercialisation

Focusing on a biomarker informed subpopulation is not necessarily the best solution from a commercialization perspective. If the product is shown to be good in all patients, but better in some, the optimal strategy may depend on the availability of diagnostic testing, the willingness of physicians to adopt the test proposition, and the willingness of the payer to pay a value-based price premium

22

Integrating Molecular Diagnostic Testing Into Routine Clinical Practice

There are many barriers to this that need to be overcome, including: Funding, Access, Testing methods and process, Test performance, Population selected, Physician adoption, Patient demand, and Conversion rate

23

When, And In Whom, To Undertake Biomarker Testing

Academic guidelines are often split between recommending comprehensive genomic profiling for all, as early on as possible, and reserving these for later-line patients. From a manufacturer's perspective a key question with impact on price, uptake, and revenues

Personalisation (2)

24

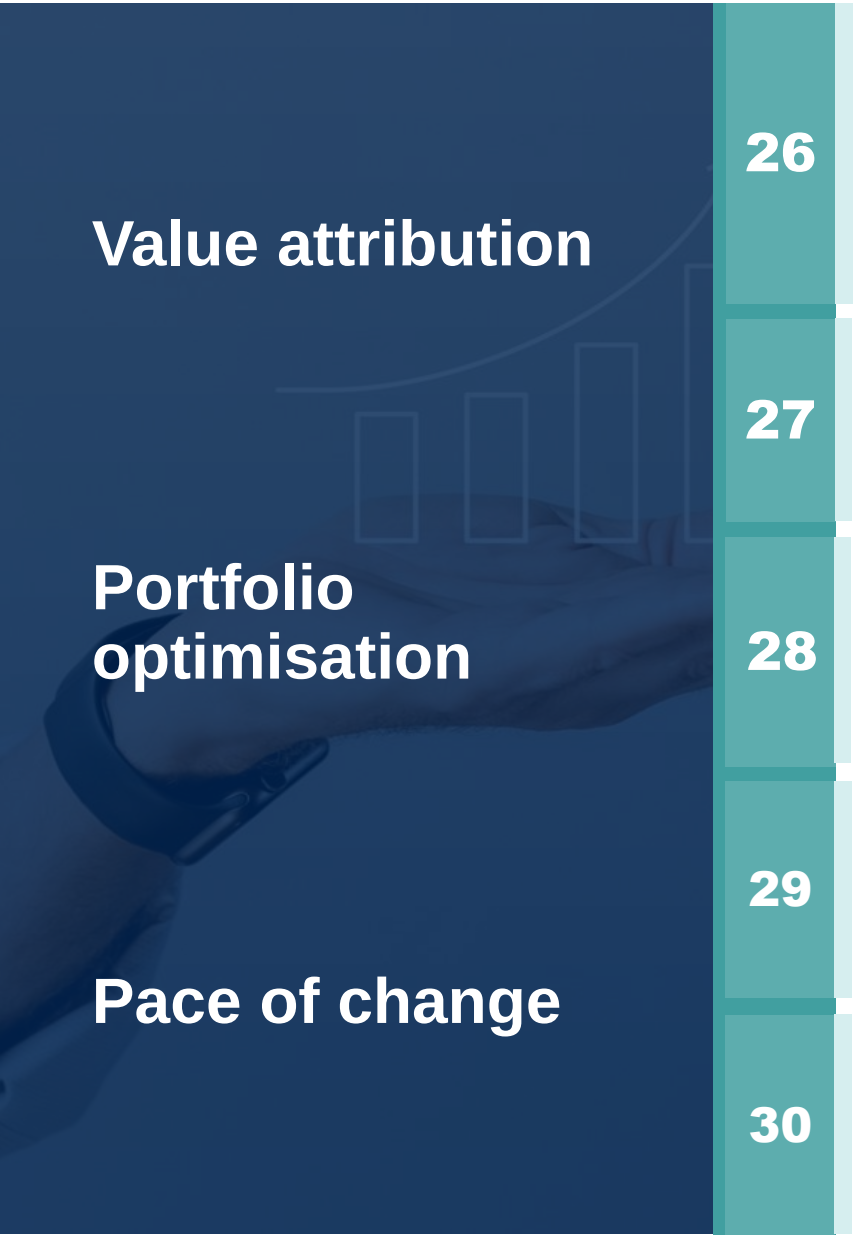
25

Keeping Up With The Science

The cost of comprehensive molecular/genomic testing will drop and the number of test providers will increase.. Physicians and payers will need to change behaviours, adopt new practices, keep up with clinical recommendations and reimbursement/coverage.

Digital Pathology

Adoption of digital workflows, digital pathology / digital diagnostics solutions. Keeping up with AI, machine learning, inter-connectedness, and information-sharing that digital pathology will allow. Challenge to incorporate diagnostics and digital pathology more closely into clinical trial design.



Value attribution

Portfolio optimisation

Pace of change

26

Cost Effectiveness

Different levels of cost-effectiveness in different indications will require new approaches to price ring-fencing. Therapy stacks of high value / high price products will also bring cost-effectiveness challenges requiring new approaches to differential and adaptive pricing. Attributing value to the individual components will key to successful negotiation.

27

Fair Allocation Of Reimbursement

Fairly reimbursing value contribution in a world where digital health and genomics / biomarker informed disease management become more closely connected. “How much should be paid by whom for what” will become a predominant health policy issue

28

Moving From The Value Of The Brand To The Value Of The Portfolio

Assessing costs and consequences of treatment strategies involving several of a company’s assets. Marketing disease management solutions. Ensuring full compliance to ensure no inducement to prescribe

29

Differing paces for technology and pharmaceutical development and approval

The development of healthcare systems and pharmaceuticals move at a glacial pace compared to the rapid development of technology, running the risk that by the time a technology is assessed, approved, and granted access, it is out of date

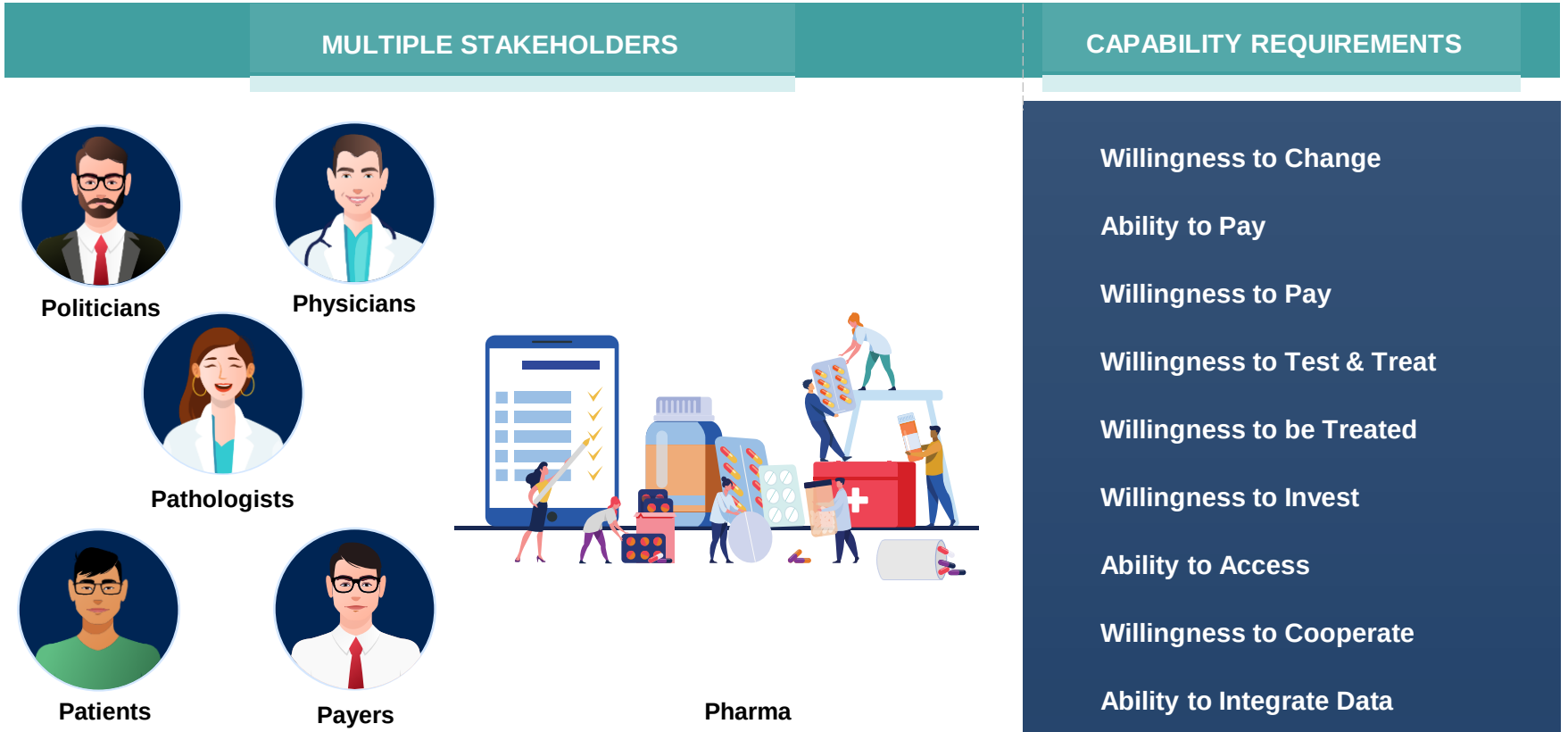
30

Corporate, Political And Societal Amnesia

There are very few challenges that are new. Companies forget that! Much can be learned from how these challenges were addressed, both successfully and unsuccessfully, in the past via analogue analyses.

Observations

- The majority of the 30 specific challenges are applicable to most therapy areas.
- The largest cluster (7/30) comprised personalisation challenges (genomic and digital linked to therapeutic).
- The 30 challenges involve multiple stakeholders and capability requirements.
- **The challenges cannot be solved in isolation, in a single company or departmental silo, based on single data sources.**



Picture reference: Adapted from "The Power of Holistic Insights: An Ipsos POV", Teale, Franceschetti, Levent, Duncan, November 2022

03

OVERCOMING THE CHALLENGES

Evidence, pricing and access will need to be re-engineered to address four factors

Science and Technology

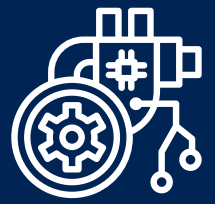
The biggest disruptor to the healthcare landscape of the future

Multi-Component Disease Management

The linking of patient-level, real-world/real-time data – together with biomarker-informed precision medicine/personalised 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 randomised controlled trials

Innovative approaches to evidence creation and pricing will be needed to overcome access & pricing challenges

Solutions

- Evidence creation: Multi-source data and modelling
- Conditional reimbursement / coverage with evidence development
- Financial and outcomes-based risk sharing
- Managed entry agreements
- Innovative funding models drawn from other industries (e.g. annuities)

Payer communication will need to have a more holistic focus

1.

Treatment sequencing

The payer value story and messaging should not be just restricted to a particular position/line in therapy. Tomorrow's payers will want much more than a selective, and arguably biased, story around a single product.

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

2.

Affordability

Cost versus value of high priced high value combinations
Companies have moved on from the simple concept that a product (the pill) has a price ($X/month). Companies in the future will be increasingly offering:

- Innovative product propositions– eg. drug/administration/ diagnostic / digital app solution packages
- Innovative pricing propositions – single lifetime Pricing, annuities etc
- Financial engineering through the apportionment of value (OHE[1])

Reference: Why We Need a New Outcomes-Based Value Attribution Framework for Combination Regimens in Oncology, Towse et al., OHE, February 2021

Payer communication will need to have a more holistic focus

3.

Predictability

- Payers will increasingly value both clinical and economic predictability – in some cases almost as highly as, or 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.

4.

Clinical endpoints & outcomes

- Classical oncology clinical outcomes (e.g. median OS) will be less dominant in the cancer immunotherapy and personalised healthcare world. Endpoint metrics that are predictive of outcome will resonate more strongly with payers
- Increasingly, payers will be faced with an array of metrics. Linking payer education with payer value messages will be necessary.

Personalisation

Eight barriers to molecular diagnostics and five to therapy use will need to be removed for biomarker driven healthcare to be successful

Barriers to molecular diagnostic use may include:

- Funding
- Access to and availability of testing
- Testing methods and process: difficulty of obtaining sample, complexity, and turnaround time
- Test performance: will the test be (or be perceived to be) insufficiently accurate or ambiguous?
- Population selected for testing: will the population tested be as broad as the drug's indication?
- Physician's adoption of the test proposition
- Patient demand for testing, and willingness to be tested
- Conversion rate: will physicians prescribe other drugs despite a "positive" test result?

Barriers to therapy use may include:

- Affordability, access and availability: of drugs, diagnostic testing, reimbursement, and of data/evidence
- Timing: delays in updating treatment guidelines, delays in Health Technology Assessments and implementation, and time lag in adopting technology
- Preference: influenced by context, personal experience, and outcomes of earlier treatment(s)
- Policy & priorities
- Power: Physician vs. payer, HTA vs. medical society, and treatment guideline perspectives differing from patients' perspectives.

Reference: Adapted from "The Power of Holistic Insights: An Ipsos POV", Teale, Franceschetti, Levent, Duncan, November 2022

Personalisation

The key challenges need to be addressed for digital health technology to be successful

The first challenge: speed of evolution

Technology is evolving faster than the regulatory, behavioural, healthcare funding, and health technology assessment (HTA) systems that are required for successful implementation.

For digital health to deliver on the promise, developers will need to produce relevant robust evidence regarding the technology for assessors; systemic changes will be required in regulatory and HTA assessment systems; the roles of the physician and data in disease management, payment systems, and the pricing of healthcare will need to change.

The second challenge: evidence

There are various challenges to evidence development in this environment, including:

- Relevance, robustness, and rigor
- Difficulty and cost of evidence development
- Timeliness of evidence delivery
- Continued validity of evidence in a rapidly evolving environment
- Measurement and attribution of co-dependent value between developers of the different disease management components.

The third challenge: value

Value will be attributed and assessed in different ways:

- Value contribution of 3 different elements: monitoring, intervention & prediction (the MIP paradigm).
- Value segmentation based on 3 outcome types: economic, clinical & humanistic
- Value perception based on 3 stakeholder groups: patient, payer & physician
- Value attribution, informing value-based reimbursement allocation, which will become increasingly important as stakeholders adopt more holistic disease management.

Reference: The Monitor Intervene Predict Value Framework, Teale, ISPOR Value and Outcomes Spotlight, January 2023

Financial engineering will be needed to address the challenges of gene, and other therapies, with high price density

Gene therapy presents specific challenges

- Cost and affordability
- Funding flows
- Uncertainty: Absence of data around long term benefit
- Value definition

Cost is the biggest concern

The cost of these therapies can be extremely expensive (in the range of $4000,000 to $1,000,000 at the high end). Budget impact could be amplified depending on the size of the patient population.

A further challenge is the timing of the cost. The fact is that all or most of the costs are upfront, not borne over time, as with chronic treatment.

Uncertainty around long-term benefit

The pathway to approval of gene therapies (especially if expedited) may yield shorter-term data on efficacy than is needed to prove the long-term therapy benefits. This results in great uncertainty around how long the therapeutic benefit will last and whether a single does will be sufficient to provide a cure. This impacts payers' willingness to pay and ability to pay limited by the 'traditional' model of short-term budgets.

Defining value

Payers may have to incorporate measures of value to patients, the healthcare system, and society in the standard value assessments, beyond normal evaluations. Additional metrics include: disease severity, age of onset, lifetime burden of the illness and informal care elements, such as returning to work or study, increases in productivity and reductions in burden of care.

Ref: EPA Congress 2021: Pricing & Access Challenges in the absence of data. Teale et al.

New payer-types will emerge and funding flows will need to change to relieve financial pressures

Gene therapies create significant administrative and financial pressures for providers.

Billing and coding issues can be burdensome and complex and can cause significant delays for the patient.

Payers encounter additional financial pressure in the form of mark-ups from hospitals or specialised treatment centres, which can be a percentage of the payment in addition to the cost of the therapy itself.

One option is for payers to purchase the gene therapies directly from the manufacturer or pay the manufacturer directly, to avoid the mark up.

Payment options for gene therapies

Traditional financial mechanisms to pay for pharmaceuticals are not adequate for gene therapies. Alternative payment models, more common to the financial services sector, will be increasingly adopted:

Any one, or combination, of these models have the potential to incentivise payers to invest in a gene therapy that may produce a better health outcome and lower cost over time, as opposed to paying for a competing product that is administered, with higher long-term costs – or even with a larger one-time/upfront costs for a curative therapy.

Ref: Ipsos Webinar The Future of Market Access, 2020

Non-comparative data, plus modelling solutions, will increasingly be required where RCTs are not ethical or feasible

RCTs aren't always ethical, feasible, or practical

A placebo/comparator is likely to be less effective than the evaluated intervention under evaluation (e.g. 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.

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

New methodologies will need to be applied to help decision-makers understand drivers of change

Modified Porter Analysis

How the forces of competition, power of buyers/suppliers & threat of substitutes influence decisions & outcomes.

STEEPLE frameworks

Social, Technological, Economic, Environmental, Political, Legal & Ethical considerations

Delphi Method

A structured approach to expert opinion, achieving consensus & highlighting areas of misalignment

Multiple Data Source Integration (MSDS)

How data & insight from many sources can be merged to inform decision-making

Behavioural Science & Prospect Theory

How behaviours influence decisions & outcomes, and how experience, uncertainty & risk change preferences

System Dynamics

Understanding the dynamic behaviour of complex systems & the relationships between the component parts

War Gaming / Competitive Simulation

Experiential methodology to guide decision making in a dynamic competitive rapidly changing environment

Stakeholder Tracking

Monitoring how differentiation & investment impacts multi-stakeholder perceptions, behaviours & outcomes

Reference: "The Power of Holistic Insights: An Ipsos POV", Teale, Franceschetti, Levent, Duncan, November 2022

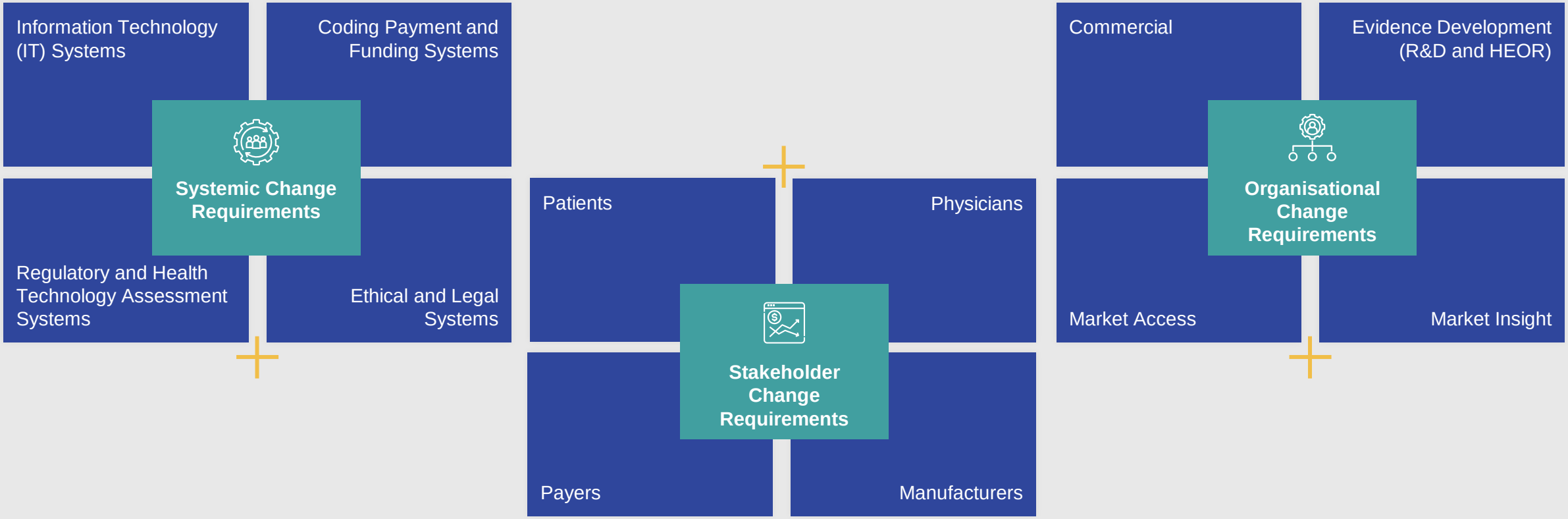
04

IMPLEMENTATION

There are (at least) three critical factors / facilitators for successful implementation of solutions

1. **CHANGE – Systemic, Stakeholder, Organisational**
2. **COLLABORATION – Between Stakeholders**
3. **INTEGRATION – Of Data from Multiple Sources**

Fundamental changes will be required to overcome the evidence availability, accessibility, and acceptability challenge



Ref: Adapted from "The Power of Holistic Insights. An Ipsos POV" Teale, Franceschetti, Levent, Duncan, November 2022

Strategic collaboration between manufacturers and data providers will be needed to access data

Through such relationships, manufacturers can more readily access comprehensive RWD which they can utilise across their portfolios

Examples

2016 — AstraZeneca becomes a Founding Enterprise Partner for CancerLinQ.

2017 — Roche acquires Flatiron Health, granting them access to 2.2 million active patient records.

2018 — Aetion and FDA enter partnership to replicate 30 published RCTs with RWD analyses.

2019 — Aetion & Cegedim Health Data announce partnership to integrate Cegedim's European RWD to Aetion's Evidence Platform which analyses RWD including claims, electronic health record & registries.

2020 — ConcertAI and Novartis enter collaboration to use RWD with three key objectives: 1) Improved RCT design 2) RWD-based label extensions & new indications 3) Accelerated market access

2021 — AstraZeneca publishes RWE study results conducted with CancerLinQ titled 'Real-world clinical outcomes of patients with BRCA-mutated (BRCAm) HER2-negative mBC'1.

2022/3 — Multiple Artificial Intelligence collaborations

Integration of data from multiple sources will be required

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 utilisation (HRU)
- Claims data
- Real-time / wearable data
- Social media data

Manufacturer's Internal Data

- Customer relationship data (CRM)
- Internal resource allocation

Reference: Ipsos Multi Source Data Strategy

In summary

- The greatest number of challenges and opportunities in 2023-30 will lie in the personalisation of healthcare (the integration of digital, genomics, and analytics).

- More and more alternative, often unstructured, data sources will be available and acceptable to use.
- Increased levels of collaboration will be required to access these.

- Significant systemic, stakeholder, and organisational barriers will need to be overcome in order to successfully address evidence, pricing & access challenges in all therapy areas in 2023-30.

THANK YOU.

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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

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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 on the European Oncology and Personalised Healthcare (PHC) thinking 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).