WORKSHOP SYNOPSIS

High public health impact medicines for chronic diseases – Do regulatory, HTA and payer paradigms need to change?

12-13th June 2025
Hyatt Regency Hotel,
Tysons Corner, Virginia, USA

CIRS Centre for Innovation in Regulatory Science

GRAPHIC SUMMARY

Common chronic diseases: A global health challenge

Example conditions:


Respiratory


Metabolic


Diabetes


Cardiovascular


Neurological

Key challenges:

- High mortality rates
- Economic burden
- Limited treatment options

A CIRS workshop involving


Pharmaceutical companies


Regulators


HTA agencies


Payers


Patient organisations


Academics

Calls for new adaptive, collaborative, patient-centered approaches to chronic disease treatment development, review and reimbursement.

What needs to change?

- Improve clinical trial efficiencies through novel trial designs and digitalisation.
- Promote company-regulator-HTA collaboration through early scientific advice and data sharing initiatives.
- Establish stakeholder expectations around the strength of the relationship between surrogate endpoints and clinical outcomes.
- Implement incentives for R&D in neglected chronic disease areas.
- Explore adaptive regulatory pathways and innovative pricing and payment models for common chronic diseases.

Background

In recent years, life expectancy has declined in affluent countries, particularly the US. While COVID-19 played a significant role, common chronic diseases—such as diabetes, cardiovascular, respiratory, metabolic, and neurological conditions—are major contributors. Despite their widespread impact, drug development for these diseases remains limited, with low success rates and fewer regulatory incentives compared to areas like oncology, rare diseases, and vaccines.

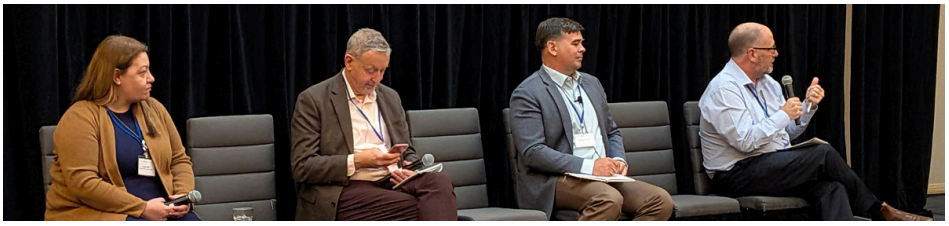
Recently, development efforts for common chronic diseases have shifted towards therapies that can prevent or slow down disease progression, rather than simply treating symptoms. Early treatment with such disease-modifying therapies could have a great impact on public and individual health. However, there are significant regulatory and reimbursement barriers to overcome due to high uncertainty around small effect size, a lack of validated biomarkers and variable disease progression.

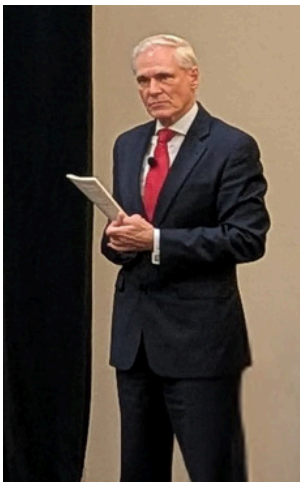
To help address these issues, CIRS convened a multi-stakeholder workshop involving industry, regulators, HTA agencies, payers, academics and patient organisations. The aim was to identify key challenges and explore solutions for improving the drug development paradigm for common chronic diseases.

Workshop format

This multi-stakeholder workshop consisted of a series of plenary sessions (see programme), featuring presentations and panel discussions that explored the current landscape including key challenges and emerging opportunities.

In addition, there were three parallel breakout discussions, guided by questions prepared by CIRS. These sessions aimed to generate actionable recommendations for improving clinical development, regulatory review, HTA assessment, and reimbursement models for chronic disease treatments.



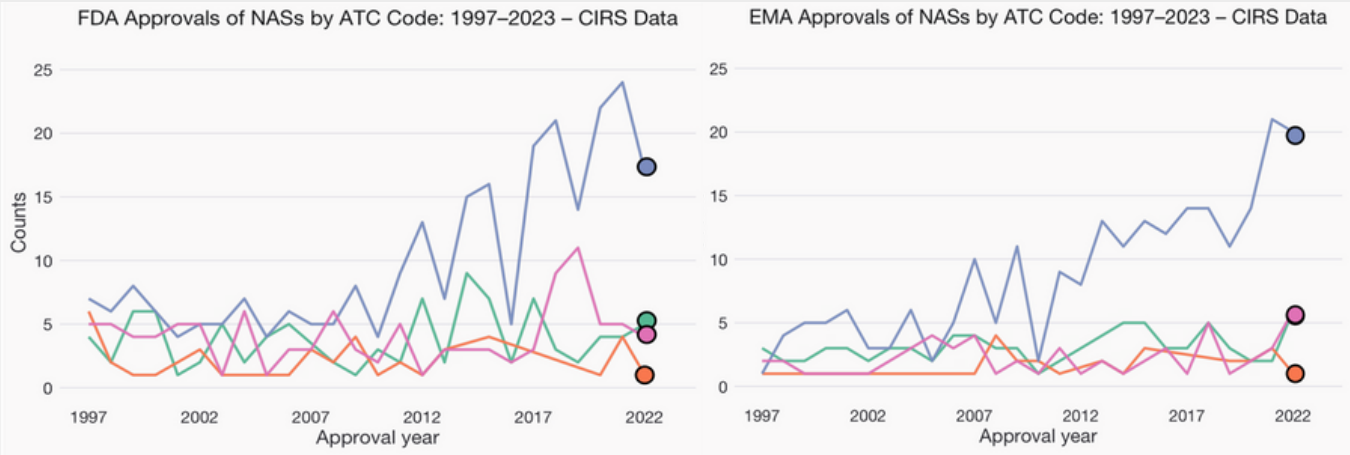

Key points from plenary sessions

Evaluating the chronic disease landscape with CIRS metrics

CIRS routinely collects publicly available data from regulatory and HTA agencies to evaluate assessment timelines for new active substances (NASs). Since 2011, the number of FDA and EMA approvals for anti-cancer and immunomodulatory NASs has outpaced those for elementary metabolism, cardiovascular, and nervous system therapies (see below). This disparity may reflect the greater availability of incentives and facilitated regulatory pathways in oncology compared to other chronic disease areas. In addition, across various countries, the time taken from regulatory submission to first HTA recommendation tends to be shorter for anti-cancer and immunomodulatory NASs than for metabolic or cardiovascular NASs (though this is driven by faster regulatory rather than HTA timelines).

CIRS data also demonstrates the positive impact of collaborative regulatory models in accelerating the availability of innovative medicines. For example, oncology NASs approved via Project Orbis showed faster median rollout times – primarily due to reduced submission gaps - compared to those not included in Project Orbis. This prompts the question of whether regulatory collaborative models like Project Orbis could be adapted or expanded to accelerate registration of treatments targeting common chronic diseases.

Are approvals skewed towards cancer due to facilitated development and regulatory pathways and incentives?



Source: CIRS datasets

Enabling flexibility in clinical development and evidence generation

Clinical trials for common chronic diseases face several challenges, including difficulties measuring subtle changes in disease progression, selecting appropriate endpoints and biomarkers, variable disease progression with frequent comorbidities, patient recruitment challenges and high costs due to large patient numbers and long trial durations. Investing in patient engagement and research to better understand disease natural history, molecular mechanisms and targets are key to establishing better endpoints that are meaningful to patients.

There is a need to embrace innovation in the form of novel trial designs, such as decentralised, hybrid and adaptive trials, and digital technologies that can reduce patient burden e.g. wearables and enhance data analysis such as AI. The platform approach could potentially improve efficiency in chronic disease development by allowing developers and regulators to leverage information across multiple products. Real-world evidence (RWE) is also important to supplement evidence from clinical trials.

Learnings from the chronic obstructive pulmonary disease (COPD) field highlight the need for multi-stakeholder collaboration to shift the focus towards earlier intervention to prevent disease progression. Progress in Alzheimer's disease illustrates how biomarkers can be used to support early therapeutic intervention, yet there are still challenges with demonstrating the relationship between surrogate endpoints and clinical outcomes.

Adapting regulatory processes and practices

Regulatory challenges for common chronic diseases include: the increased use of surrogate endpoints, which may not clearly demonstrate clinical outcomes and thus increase uncertainty in evidence; more personalised treatment approaches; and differences in benefit-risk expectations due to the typically slow progressive nature of these diseases.

While the regulatory system has evolved to expedite rare disease and oncology drugs, medicines for chronic diseases have been neglected: they lack the sort of incentives available for orphan drugs and rarely qualify for facilitated or expedited regulatory programmes. This creates a misalignment in public health policy, as drugs that could modify prevalent chronic diseases at early stages could potentially have greater societal and economic impact than some oncology and rare disease treatments.

Therefore, the current regulatory model for common chronic diseases needs to evolve and become more flexible. Potential improvements to consider are:

- Using adaptive approval pathways and rolling reviews.
- Being more open to surrogate endpoints and RWE.
- Reviewing existing pathway criteria to better reflect and address health system needs.
- Leveraging learnings from collaborative assessments, including Project Orbis and the Access Consortium.
- Engaging in early and iterative dialogue with other regulators, industry and HTA agencies.
- Increasing collaboration with HTA agencies on surrogate endpoints and patient engagement.
- Strengthening the integration of patient experience data and patient-reported outcomes in decision making.

Evolving HTA and payer frameworks

Early large-scale adoption of innovative treatments for common chronic diseases faces substantial technical and financial hurdles. Some innovations require changes to delivery models and infrastructure that are difficult to quantify in cost-effectiveness analyses. The interplay with supportive services e.g. for behavioural and lifestyle changes, is also difficult to determine. Horizon scanning may help to give HTA agencies and payers more sight of these issues before making coverage decisions.

While surrogate endpoints can be valuable for initial approval of treatments for common chronic diseases, HTA agencies and payers ultimately require evidence of direct effects on patient-centric outcomes. Increased reliance on surrogate endpoints and less mature evidence creates uncertainty around cost-effectiveness estimates. Outcomes-based agreements, such as managed access arrangements, can help mitigate this, but may necessitate investment in health data infrastructure to capture robust data.

Establishing and communicating expectations around the strength of relationships between surrogate endpoints and clinical outcomes is crucial, requiring collaboration between regulators, HTA agencies and payers.

Cost-effectiveness comparisons can be skewed when generic drugs are used as benchmarks. For example, novel non-opioid analgesics may appear less viable when compared to morphine on a dollar-per-dose basis. A broader definition of value and agreement on appropriate comparators are needed.

Affordability is a key issue for HTA agencies and payers, given the large chronic disease patient populations that could be eligible for early-stage treatment. Exploring innovative pricing and payment models and identifying patient subgroups most likely to benefit from treatment may help to tackle affordability issues.

Broader elements of value, such as productivity, social care costs, and caregiver burden, should be incorporated into HTA and payer frameworks. However, robust data on these aspects is not always available at the time of assessment.

Finally, for payers, patients moving between insurance providers creates challenges for evaluating long-term outcomes, as the payer initially covering a treatment may not see its future health and cost benefits.

Keeping patients at the centre

For some chronic diseases like COPD, development approaches have remained largely unchanged for decades, and so approvable endpoints are not aligned with patients' primary concerns. Despite effective existing treatments, many patients remain unsatisfied and want new options. To successfully change this paradigm, patients should be involved earlier in development processes and all stakeholders must work together while considering patient perspectives.

While the value of patient involvement is broadly recognised, often less consideration is given to how patient input is integrated throughout development, regulatory, HTA and payer processes. It is important to distinguish between different types of patient input; for instance, patient perspectives on areas of unmet need and drug development can differ significantly from patient preferences or patient-reported outcomes.

When involving patients, clarity is essential. Stakeholders should be clear about the type of information they are seeking — whether it's about lived experience, day-to-day expenditures, barriers to receiving care or treatment, or treatment experiences.

There is often a perception issue of potential conflicts of interest when engaging with patients. However, when clear parameters are in place to protect all parties, meaningful discussions can take place.
In addition to individual patients and patient groups, valuable insights can be gained from collaborative partnerships with organisations representing multiple disease communities, such as the American Brain Coalition.

Advancing research in women

Women experience a higher prevalence than men of many chronic conditions, including hypertension, arthritis, and dementia. However, research to understand these differences is limited, contributing to poorer health outcomes for women and substantial costs to individuals and society. The National Academies Committee on a Framework for the Consideration of Chronic Debilitating Conditions in Women has recommended a research agenda focused on:

- Better data, better biology - Need for better data collection, surveillance, biological models that reflect women's bodies.
- Improving care pathways - Challenges in diagnosis, treatment, and managing multiple chronic conditions in women.
- Understanding lived experience - How trauma, identity, and inequities shape health; need for women-centered, inclusive research.

Is it time for a shift in the development paradigm?

There is no doubt that common chronic diseases have been underserved in recent years, despite posing a major global health challenge. These conditions are associated with high mortality rates, significant economic burden, and limited treatment options.

Addressing this challenge requires more than incremental change — it demands a fundamental reimagining of how treatments are developed, evaluated, and brought to market.
A more **adaptive**, **collaborative**, and **patient-centered** approach is urgently needed, with **targeted incentives** playing a central role.

Recommendations from breakout discussions

Clinical trials – How should the thinking be reframed for undertaking clinical trials for high impact chronic diseases?

- Increase collaboration across stakeholders, including patients, regulators, payers, HTA agencies, sponsors, and clinicians, through early dialogue e.g. scientific advice, and pilots to move initiatives forward.
- Improve clinical trial efficiencies by:
  - Focusing on understanding the early trajectory of the disease and the patient perspective, making use of technological enablers e.g. AI, wearables.
  - Identifying appropriate surrogate biomarkers and establish their efficacy.
  - Embracing pragmatic and decentralised trial (DCT) designs.
  - Harmonising endpoints globally.
- Explore 'clinical research as a care option', where trials procedures can be regarded as usual care and reimbursable through health care provision. This could be facilitated by delivery networks or public-private set-ups.
- Explore adaptive approval and reimbursement models to allow early entry for initial indications, provided there is a clinically relevant effect size, while label extension/variations are being addressed in the next wave of studies that involve DCT/pragmatic trial elements.
- Promote use of RWE, exploring regulators' requirements and acceptance of evidence from electronic health records.

How should regulatory and HTA frameworks evolve to incentivise and enable development for high impact chronic diseases?

- **Financial incentives** - Implement tax credits, grants, vouchers, subsidies and/or patent extensions to incentivise R&D in neglected chronic disease areas.
- **Adaptive regulatory pathways** – Introduce accelerated approval mechanisms that incorporate RWE and patient-reported outcomes (PROs).
- **Flexible trial design** – Encourage innovative trial designs, such as adaptive or pragmatic trials, to improve efficiency and cost-effectiveness.
- **Multi-stakeholder collaboration:** Promote company-regulator-HTA collaboration through early scientific advice and data sharing initiatives.
- **HTA/payer predictability:** Establish clear and consistent guidelines for the types of evidence needed to help streamline reimbursement and improve patient access.
- **Dynamic pricing:** Investigate dynamic pricing as a way to incentivise development for chronic diseases.
- **Medical guidelines:** Update medical guidelines for chronic diseases more frequently to avoid delays in the adoption of new treatment approaches.
- **Priority setting:** Establish national health targets to provide clear signals of priorities and unmet needs, helping to inform investment decisions.

Recommendations from breakout discussions (continued)

How to address the regulatory, HTA and payer challenges for therapeutics that slow or prevent disease rather than merely act on symptoms?

Development

- Use platform review and early consultation.
- Place a higher valuation of societal impact, PROs and healthcare resource utilisations in trial design.
- Increase emphasis on disease sub-populations and improve understanding of underlying pathophysiology.
- Consider running a natural history cohort/external control arm in addition to RCTs to help address potential evidence gaps.

Regulatory review

- Leverage existing RWE frameworks e.g. Data Analysis and Real World Interrogation Network (DARWIN EU), FDA RWE programmes.
- Elicit patient-centric value of 'delay/prevention'.
- Include clinical outcome assessments/PROs in the label.
- Consider the appropriateness of surrogate endpoints and the possibility of offering longer market exclusivity if product approval is delayed to accommodate longer-term data collection.
- Adapt existing frameworks to prioritise high impact chronic diseases.

HTA/reimbursement

- Review the appropriateness of current HTA methodologies for evaluating treatments delaying disease onset or progression.
- Consider using alternative reimbursement models e.g. subscription model, Per Member Per Month, Pay for Performance, including the potential for re-evaluation of access decisions based on longer-term data or RWE.

Recommendations for CIRS from across the breakout groups:

- Facilitate a multi-stakeholder study to investigate unmet medical needs for chronic diseases from the patient's and caregiver's perspective.
- Conduct a landscape analysis on the effectiveness of tax credits, funding models, and market exclusivity in stimulating R&D investment in chronic disease innovation.
- Review existing research on alternative payment models including managed entry agreements and survey CIRS members to assess whether these models work and how they could be improved.
- Analyse the current global landscape for joint scientific advice, including learnings, recommendations and potential for expansion into the US.
- Convene multiple stakeholders to develop policy solutions for the lack of progress in the consideration of patient-centred outcomes, PROs and societal benefits in regulatory, HTA and payer decision making.

Workshop programme

Session 1: The impact of chronic disease on health systems and life expectancy - Current landscape and challenges	Session 2: Enabling flexibility in clinical development and evidence generation for high impact chronic diseases
Chair: Prof Hans-Georg Eichler, Consulting Physician, Association of Austrian Social Insurances	**Chair: Prof Hans-Georg Eichler,** Consulting Physician, Association of Austrian Social Insurances
Dr Neil McAuslane, Scientific Director, CIRS **Jeffrey Francer,** Vice President, Head of Global Regulatory Policy and Strategy, Eli Lilly, USA **Dr Nick Crabb**, Chief Scientific Officer, National Institute for Health and Care Excellence (NICE), UK **Dr Bruce Miller**, Chief Scientific Officer, COPD Foundation, USA **Vicky Brown**, Associate Vice President, Clinical Drug Safety, Humana, USA **Prof Tony Lawler**, Deputy Secretary, Health Products Regulation Group, Australian Government Department of Health and Aged Care **Kelly Robinson**, Director General, Pharmaceutical Drugs Directorate, Health Canada	**Prof John Skerritt**, Enterprise Professor for Health Research Impact, University of Melbourne, Australia **Alexis Reisin Miller**, Head, Global Regulatory Policy, Merck, USA **Prof Ton de Boer**, Chair, Medicines Evaluation Board (MEB), The Netherlands **Dr Daniel Ollendorf**, Chief Scientific Officer and Director of HTA Methods and Engagement, Institute for Clinical and Economic Review (ICER), USA **Bisola Filchak**, Vice President, Immunology and Inflammation, Global Regulatory Affairs, Sanofi, USA **Simon Bennett**, Global Regulatory Policy, Biogen, UK
Session 3: Adapting regulatory and HTA process and practices for high impact chronic diseases	**Session 4: Breakout discussions - Priority research areas and how to address policy challenges**
Chair: Dr Supriya Sharma, Chief Medical Adviser, Health Canada	**A) How should the thinking be reframed for undertaking clinical trials for high impact diseases?** **Chair: Kelly Robinson,** Director General, Pharmaceutical Drugs Directorate, Health Canada **Rapporteur: Dr Odd Erik Johansen,** Principal Medical Director, Roche, Switzerland **B) How should regulatory and HTA frameworks evolve to incentivise and enable development for high impact chronic diseases?** **Chair: Prof Ton de Boer**, Chair, MEB, The Netherlands **Rapporteur: Michael Cunha**, Senior Director, Regulatory Policy & Science, Bayer, USA **C) How to address the regulatory, HTA and payer challenges for therapeutics that slow or prevent disease rather than merely act on symptoms?** **Chair: Prof Hans-Georg Eichler,** Consulting Physician, Association of Austrian Social Insurances **Rapporteur: Alix Arnaud,** Global Market Access Strategy and Operations Lead, Sanofi, USA
Dr Melissa Laitner, Director of Strategic Initiatives, National Academy of Medicine, USA **Ginny Beakes-Read**, Vice President and Head, Global Regulatory Policy, Johnson and Johnson, USA **Dr Eveline Trachsel,** Head of Medicinal Products Approval and Vigilance, Member of the Management Board, Swissmedic **Dr June Cha,** Director, Policy, Milken Institute, USA **Paul Villa,** Disease Area Head, Respiratory Global Pricing and Market Access, GSK, USA **Dr Sahar van Waalwijk van Doorn-Khosrovani,** Member of the National Funder's Committee for Evaluation of Specialised Medicines and Companion Diagnostics, CZ, The Netherlands **Jessica Daw,** Vice President, Pharmacy, Sentara Health Plans, USA	
Session 5: Panel discussion - Policy actions/considerations	
Chair: Dr Brian O'Rourke, Chair, CIRS HTA Steering Committee	
Andrew Emmett, Vice President, Global Regulatory Policy and Intelligence, Pfizer, USA **Prof Tony Lawler,** Deputy Secretary, Health Products Regulation Group, Australian Government Department of Health and Aged Care **Dr Daniel Ollendorf**, Chief Scientific Officer and Director of HTA Methods and Engagement, ICER, USA **Leslie Ritter,** Vice President, Healthcare Access, National MS Society, USA, and Board Member and Advocacy Chair, American Brain Coalition	

About CIRS

The Centre for Innovation in Regulatory Science is a neutral, independent UK-based subsidiary of Clarivate plc. Its mission is to maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and health technology assessment (HTA) policies and processes. CIRS provides an international forum for industry, regulators, HTA bodies and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy. It is governed and operated by Clarivate for the sole support of its members' activities. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities, and grants.

Workshop organised by

Dr Magda Bujar, Associate Director, Regulatory Programme and Strategic Partnerships, CIRS

Gill Hepton, Administrator, CIRS

Dr Neil McAuslane, Scientific Director, CIRS

Anna Somuyiwa, Head, CIRS

Dr Tina Wang, Associate Director, HTA Programme and Strategic Partnerships, CIRS

Synopsis prepared by

Dr Jenny Sharpe, Communications Manager, CIRS

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Keep in touch

Centre for Innovation in Regulatory Science (CIRS)

70 St Mary Axe, London EC3A 8BE, UK

Email: cirs@cirsci.org

Website: www.cirsci.org