Methodology Challenges to Assessing the Value of Long-Acting Treatments

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Challenges in Assessing Value of Long-Acting Therapies

- **Many payers see LA therapies as patent extensions or evergreening strategies by industry. Examples are plentiful, where LA modifications follow a successful SA product.**
- **Scepticism about the real value of long-acting treatments.**
  - What are the methodological challenges and opportunities to assess societal value, adherence impacts, and patient-centred outcomes of LA-therapies?
  - Do LA therapies actually improve treatment adherence? How to account for the adherence value of LA therapies in modelling and HTA decision making?
  - Are all LA therapies really long-acting? What about ultra long acting, for example cell and gene therapies?

Challenges in Assessing Value

- **What are the methodological challenges and opportunities to assess societal value, adherence impacts, and outcomes of LA-therapies?**
  - **Durability of Treatment Benefit -** Long-acting treatments may maintain therapeutic levels over extended periods, but evidence on long-term efficacy is often sparse or based on surrogate outcomes.
  - **Delayed Benefit -** LA treatments might show benefits (e.g., relapse prevention or reduced disease progression) only after months or years of treatment, requiring long-term studies or modeling w/assumptions.
  - **Heterogeneous Treatment Response/Risk -** Different patient subgroups may experience varying levels of benefit or risk, complicating population-level assessment.

Challenges in Assessing Value

- **Do LA therapies actually improve treatment adherence? How to account for the adherence value of LA therapies in modelling and HTA decision making?**
  - **Adherence Assumptions:**
    - Clinical trials are arguably the worst source of adherence data.
    - Models often assume improved adherence with long-acting therapies compared to daily oral options, but real-world data are often limited, especially early in a products life-cycle, to inform these assumptions.
    - Analysts will use a ‘precedent’. Most HTA evaluators don’t’ like this approach.
  - **Attribution Challenges:**
    - It’s difficult to isolate the independent value of adherence from the intrinsic efficacy of the treatment.

Challenges in Assessing Value

- **Do LA therapies actually improve treatment adherence? How to account for the adherence value of LA therapies in modelling and HTA decision making?**
  - **Time Horizon:** Long time horizons are required to measure the full benefits and costs (e.g., fewer relapses, hospitalizations), increasing uncertainty.
  - **Discounting Future Benefits:** Economic evaluations discount benefits over time, which can disproportionately reduce the perceived value of treatments with delayed or long-term benefits.
  - **Comparator Selection:** Choosing an appropriate comparator is difficult if long-acting treatments represent a new standard or paradigm shift.

Challenges in Assessing Value

- **Unique Challenges for Ultra Long-Acting Treatments – Cell and Gene Therapies?**
  - **Limited Follow-Up:** Clinical trials often have short follow-up periods relative to the expected duration of benefit, sometimes only 1–3 years for therapies promising decades of effect.
  - **Immature Survival Data:** Especially for rare or pediatric diseases, survival data are often immature, requiring extrapolation far beyond observed trial data.
  - **Uncertain Durability:** While curative claims are sometimes made, durability of treatment effect may not be known, especially for therapies targeting genetic or immune pathways with potential for relapse or requirements for therapy augmentation.

HTA Uncertainty and a Solution

HTA Value Frameworks:

- HTA value frameworks may not allow for the unique advantages of long-acting treatments within their standard comparative benefit and cost-effectiveness methods. For example,
  - Care-giver burden maybe substantially reduced with fewer trips to healthcare providers.
  - Single administration treatments may promote more interest in receiving care (e.g. for infectious disease, prevention, etc.)

Innovative Payment Models:

- Because of uncertainty, LA treatments may require alternative reimbursement approaches (e.g., outcomes-based agreements) to reflect the real value of improved outcomes.

Potential Environmental/Carbon Impacts of LA Treatments

- Fewer Materials and Packaging
- Supply Chain/Distribution Economies
- Carrying Costs/Storage Space for Wholesalers and Pharmacies
- Fewer Trips for Patients to Healthcare Providers
- Lowering Healthcare System Capacity Constraints