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Assessing the Life-cycle Value Added of Second-Generation Antipsychotics in Sweden and the UK: The Case of Risperidone

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Background

The value to society of pharmaceutical innovation depends on the long-term health and related benefits, net of additional costs.

Research to estimate long-term value added by new medicines is needed to inform price and adoption decisions[1,2]

The use of either therapeutic added value or cost effectiveness analysis to inform adoption decisions at launch is the current trend

As opposed to what is assumed in traditional CE analysis which typically considers the short- and medium-term, the value of a medicine may change in the long-run in response to several factors:

- Generic competition may reduce the price of a drug still in use[3-6]
- On-patent competition could also reduce the price and increase the value added[7-10]
- Improved (more effective) presentations of the medicine
- Marketing authorisation granted for new indications[5,11,12]

Aim

To assess the life-cycle value of innovative medicines based on the example of Second-Generation Antipsychotics (SGA)

- Estimate a proxy of the incremental life-cycle cost effectiveness of the SGA against First-Generation Antipsychotics (FGA)
- Estimate the absolute social value added by risperidone (SGA), measured by the sum of the consumer and producer surpluses

Assess the dynamics of the value added by SGA vs FGA

Methods

Countries: UK and Sweden

Indications covered: schizophrenia (with estimates for bipolar disorder and dementia)

Number of patients:

- For the UK we apportioned usage and volume data (IQVIA)[13] through weighted Defined Daily Dose (SmPC)[14]
- For Sweden, we directly obtained number of patients treated from Medical Index Sweden[15] (1994-2002) and National Board of Health and Welfare[16] (2006-2018)

Cost-effectiveness data: literature review by MB and BZ using PubMed and DARE

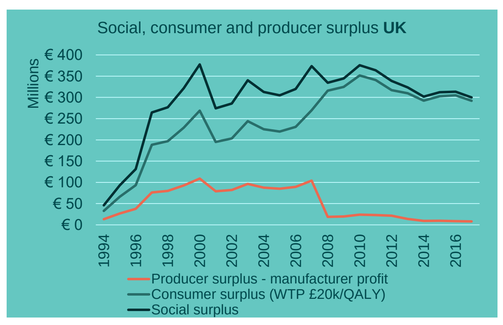
Modelling: we estimated uptake of risperidone over time (1994-2018) and attributed cost-effectiveness using number of patients treated per year

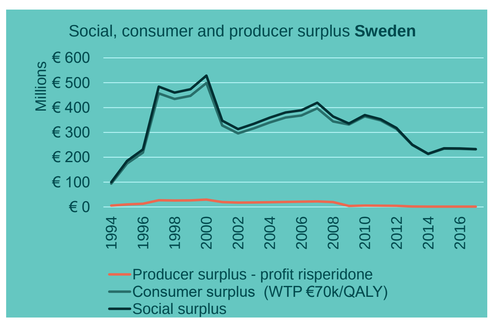
Results (1)

We performed two different general analyses for both, UK and Sweden: absolute and incremental.

Absolute analysis of the social surplus:

- Social surplus: the sum of the consumer and producer surpluses.
- Consumer surplus: the difference between the system's willingness to pay (WTP) per total QALY gain and the cost (price) of the medicine;
  - Assumed systems' WTP: £20k/QALY for the UK and €70k/QALY for Sweden.
- Producer surplus: commercial benefit obtained by the manufacturer from selling the medicine calculated as the difference between revenue – the price (cost) of the medicine per patient multiplied by the number of patients – less the (assumed) operating cost (e.g., manufacturing, marketing and distribution).

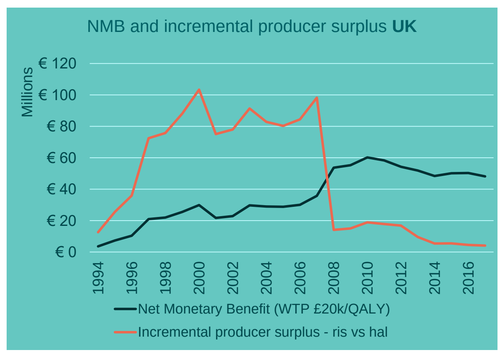


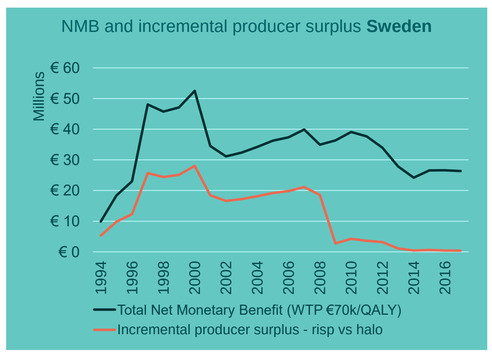


- For the UK, the producer surplus represents around 28% of the total surplus before patent expiration and around 5% after patent expiration.
- For Sweden, the producer surplus represents around 6% of the total surplus before patent expiration and around 1% after generic competition.

Incremental analysis of cost-effectiveness:

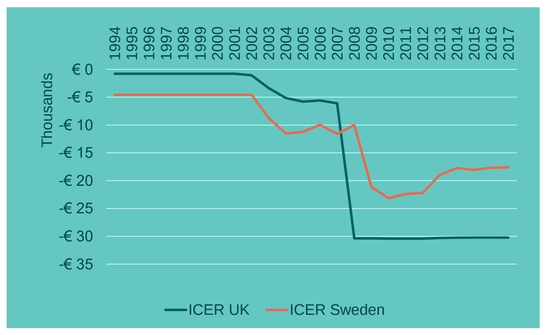
- Incremental Cost-Effectiveness Ratio (ICER): the incremental cost to incremental health gain ratio per patient.
- Net Monetary Benefit (NMB): the consumer's willingness to pay multiplied by the incremental QALY, less the incremental cost.
- Incremental surplus captured by the producer: the additional surplus that the producer of risperidone captures compared to the haloperidol producer, under the assumption that both would treat the same number of patients.





- In the UK, NMB increased (almost) continuously between 1994 and 2017:
  - Generic entry (2007) pushed NMB up from €1,043 per patient to €2,130 per patient (+104%) in period 2008-2012
  - Incremental surplus by producer dropped €3,107 per patient to €625 per patient (-80%) in period 2008-2012, just after generic entry
- In Sweden, due to the higher WTP NMB always remained above the incremental surplus captured by the producer between (1994-2017):
  - Generic entry (2009) pushed the NMB up from €3,605 per patient to €4,099 per patient (+14%)
  - Incremental surplus captured by producer dropped from €1,913 per patient to €349 per patient (-82%)

Results (2)



- ICER was negative in both UK and Sweden, for the whole period considered (1994-2017), i.e. positive health effects and cost savings.
- The launch in 2003 of Risperidone Long-Acting Injectable (RLAI) reduced significantly the ICER in both countries: mainly due to costs saved to health systems because its clinical superiority (e.g. lower relapse rate, lower hospitalisations).
- Generic entry additionally reduced the ICER in both countries, UK and Sweden, although in Sweden, the entry of Paliperidone Long-Acting Injectable (PPLAI) was more aggressive in 2013 and took back all the cost-effectiveness benefit delivered by RLAI

Discussion

Currently market access decisions are based on technology appraisals (TAs) or cost-effectiveness analyses (CEAs) focused on a medium/short-run and only for the indication covered in the marketing authorisation licence:

- The findings of the present study demonstrate that **generic competition significantly increases the value accrued by health systems and patients** (consumers) via lower prices and so lower healthcare costs
- **The launch of RLAI**, a better formulation with improved health outcomes for patients also **increased the value added to the society** (i.e., to the health system, patients, citizens and innovators) in the long-run.
- The approval of cost-effective **new indications** during the life-cycle (i.e., bipolar disorder and dementia) would have increased the value added by SGAs to the society

Caveats:

- Not fully comprehensive data on cost-effectiveness from the literature review: criteria applied to estimate transferability of results from studies.
- Data availability issues:
  - Assumptions on the commercial margin have been applied following published literature[5];
  - Assumptions on countries WTP[17,18] have been necessary to be applied with their subsequent impact on results;
  - Assumptions to fill data gaps on uptake, share of uptake between RLAI and oral risperidone and share of uptake in schizophrenia have been also applied
- Limited scope of the study: only UK and Sweden have been considered

Conclusion

- Our analysis of the life-cycle value of risperidone versus haloperidol shows that health systems and societies in general (consumers) were able to appropriate most of the life-cycle value (surplus) generated.
- The value added by the SGA significantly increased with both, the launch of RLAI and with generic competition, showing that the entire life-cycle value added by SGAs to the system is higher than the value estimated using cost-effectiveness analysis at launch.
- Consequently, we suggest that pricing and reimbursement decisions should consider the dynamic nature of pharmaceutical markets and the value added by innovative medicines over the long-run.
- There is an implementation issue as at launch huge uncertainty about the future performance of the assessed medicine which makes very difficult to take into account the value added during the life-cycle

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