

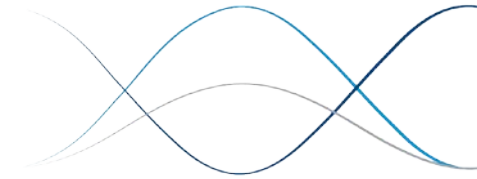
# The Expanding Value Footprint of Oncology Treatments

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Koonal Shah, Jorge Mestre-Ferrandiz, Louis Garrison,  
Adrian Towse

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# Acknowledgments

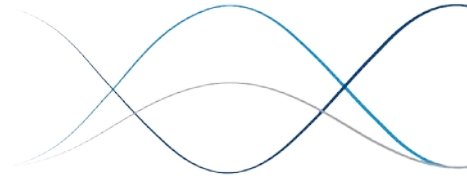
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- We also wish to thank Phill O’Neill for his contributions to the analysis of the IMS data; and to Lesley Cockroft for her review of the earlier draft.
- We are grateful to IMS Health for allowing us access to the IMS database. Any errors in analysis remain the responsibility of the authors.
- The full report can be accessed at: [www.ohe.org](http://www.ohe.org)

# Agenda

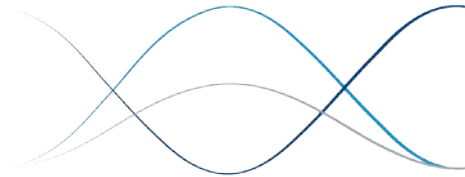
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- ✓ **Introduction and context**
- ✓ Methodology and data sources
- ✓ Tracking value expansions over time
- ✓ Analysis of data on prices, volumes and sales
- ✓ Selected discussion points
- ✓ Conclusions

# Introduction and context

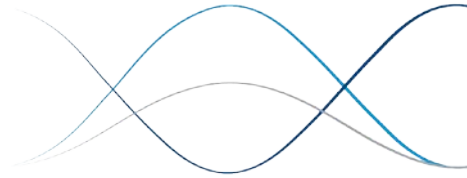
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- Cancer drugs tend to be more expensive than those used in most other therapeutic areas
- At the time of initial regulatory approval, the health outcome gains from the use of new cancer drugs are often seen as being quite modest
- Challenging HTA environment due to high costs of cancer drugs, combined with limited evidence about their impact on key health outcome measures in real-world settings
- Many new cancer drugs have a therapeutic potential well beyond their initial indication
- **The objective of this study is to provide a better understanding of how changes in the use of an oncology medicine can affect its aggregate value**

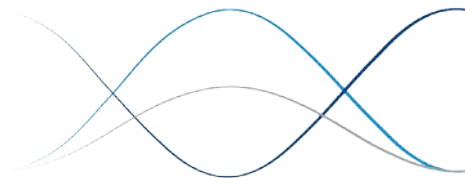
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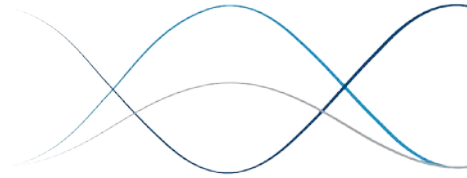
# Methodology and data sources



- Our cohort: all oncology drugs assessed by the EMA between 2003 and 2005:

Medicine	Generic name	Authorisation Holder	Status	Authorisation date	Orphan?
<b>Busilvex</b>	busulfan	Pierre Fabre Médicament	Authorised	09/07/2003	Yes
<b>Zevalin</b>	ibrutinomab tiuxetan	Spectrum Pharmaceuticals B.V.	Authorised	16/01/2004	No
<b>Faslodex</b>	fulvestrant	AstraZeneca UK Ltd.	Authorised	10/03/2004	No
<b>Litak</b>	cladribine	Lipomed GmbH	Authorised	14/04/2004	Yes
<b>Velcade</b>	bortezomib	Janssen-Cilag International NV	Authorised	26/04/2004	No
<b>Lysodren</b>	mitotane	Laboratoire HRA Pharma	Authorised	28/04/2004	Yes
<b>Erbitux</b>	cetuximab	Merck KGaA	Authorised	29/06/2004	No
<b>Alimta</b>	pemetrexed	Eli Lilly Nederland B.V.	Authorised	20/09/2004	No
<b>Avastin</b>	bevacizumab	Roche Registration Ltd.	Authorised	12/01/2005	No
<b>Tarceva</b>	erlotinib	Roche Registration Ltd.	Authorised	19/09/2005	No
<b>Yondelis</b>	trabectedin	Pharma Mar S.A.	Refused	-	No

# Methodology and data sources



- We propose a conceptual model (hierarchical framework) to set out possible value expansions beyond a given product's initial approved indication

**Initial approval** (e.g. metastatic colorectal cancer)



**Cancer type** (e.g. breast cancer)



**Disease stage** (e.g. locally advanced)



**Treatment line/stage** (e.g. first line)



**Treatment regimen** (e.g. as monotherapy, initial approval being in combination with chemotherapy)

## **Use in new route of administration**

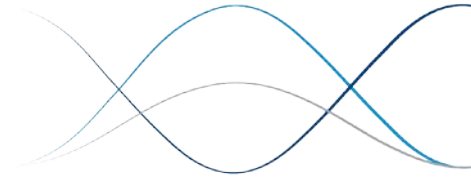
(e.g. subcutaneous as additional option to intravenous)

## **Patient sub-population**

(e.g. indicated for children or indicated only for patients with KRAS wild type tumours)

# Methodology and **data sources**

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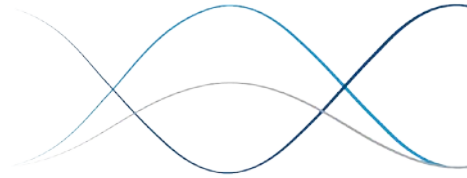


- EMA website for details of marketing authorisations
- Payer / HTA agency websites for tracking assessments and appraisals
  - NICE (England and Wales) appraisal guidance documents
  - HAS (France) assessment documents
  - Aetna (US) Clinical Policy Bulletins
- IMS for data on prices, volumes and sales



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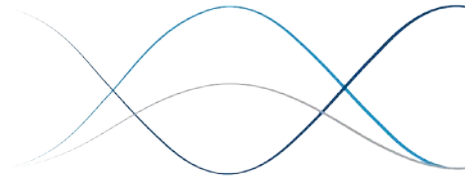
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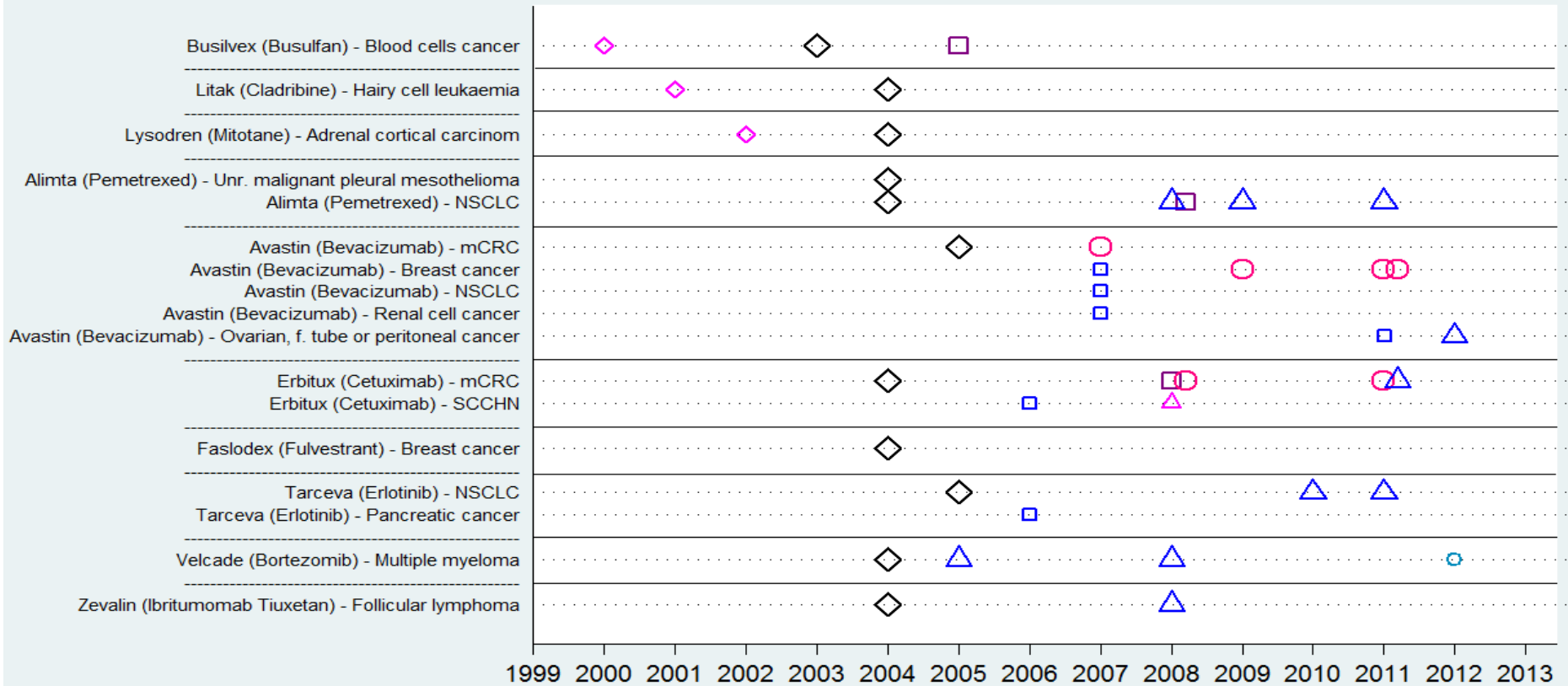
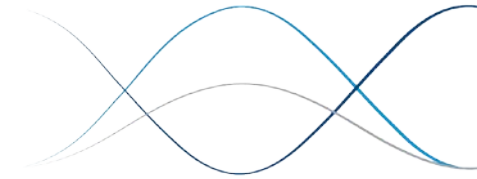
# Tracking value expansions over time

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- For each product, we identified all expansions of value since initial approval by the EMA
  - Our results are in line with previous evidence: 7 of the 10 drugs have additional value expansions beyond their initial indication
  
- We then reviewed the assessments undertaken by our three payers/HTA agencies of interest (NICE, HAS and Aetna) for each of the EMA-approved indications

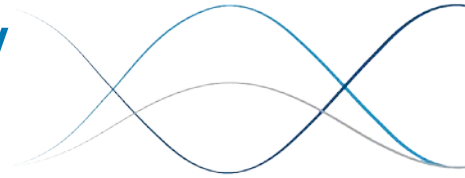
# EMA recognitions of value



- ◇ Orphan Designation
- ◇ Initial Approval
- △ Use in Different Treatment Line/Stage
- △ Use in Different Disease Stage
- Use in Different Cancer Type
- Use in Different Treatment Regimen
- ◻ Patient (Sub)Population
- Use in New Route of Administration

# Summary of payer / HTA agency decisions

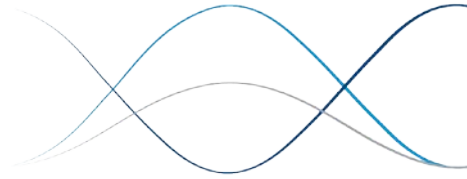
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- NICE
  - Majority of appraisals (63%) resulted in the drug/indication not being recommended for use in the NHS
  - Supplementary end of life policy meant that Alimta was recommended for use in one of its indications despite its estimated cost-effectiveness being beyond the range normally considered acceptable
- HAS
  - 80% positive recommendations
  - Most of the drugs/indications in our study were deemed as providing little or no additional value
  - Our results, supported by Drummond et al. (2014), suggest that few oncology drugs are rewarded with an ASMR of I, so many cancer drugs that reach the French market face price controls
- Aetna
  - Many decisions identified (131) but the data have important limitations

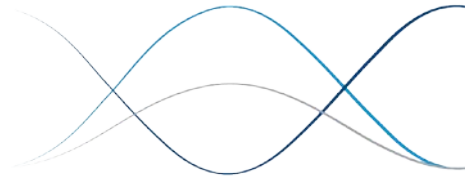
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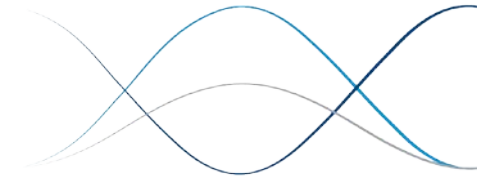
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# Analysis of data on prices, volumes and sales



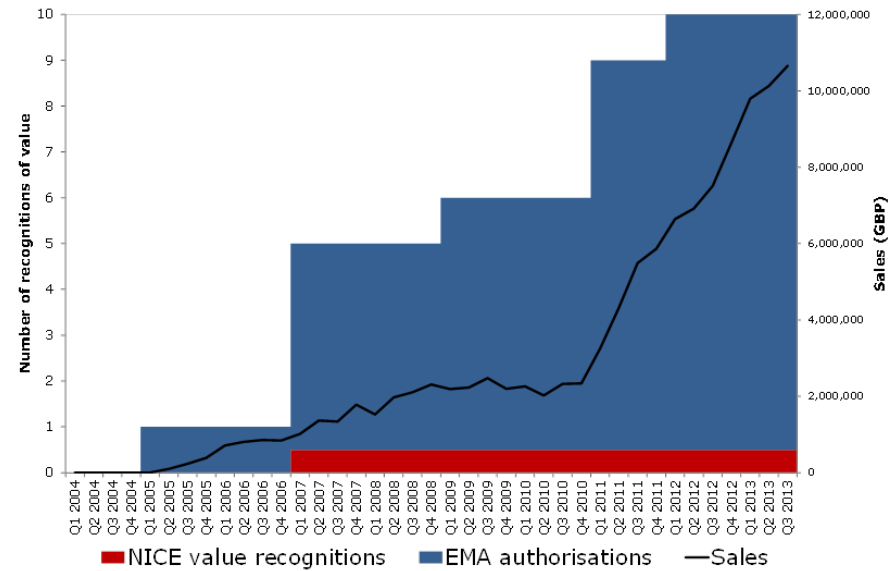
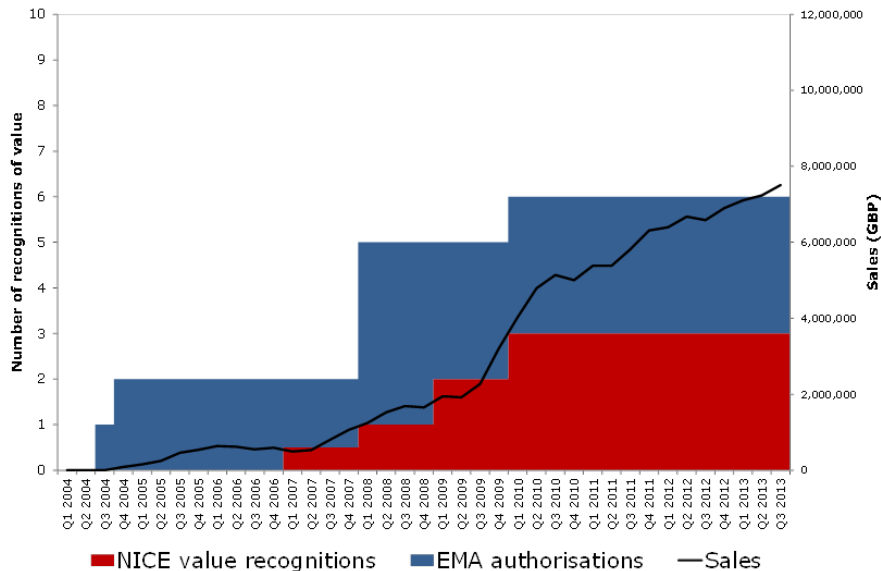
- Our analysis of the IMS data focused on the five drugs with most value expansions: Avastin, Velcade, Erbitux, Tarceva and Alimta
- Sales for these medicines represent around 95% of total sales for the 10 medicines in each country in the last year of available data
- Overall results:
  - Overall, the UK had lower prices, volumes and sales than France and the US (with three exceptions)
  - Comparisons between France and the US were a little more equivocal: for two medicines – Avastin and Erbitux – prices in France were lower than in the US throughout the study period; the opposite was true for Velcade
  - Volumes (per 100,000 people) in France were for four medicines – Avastin, Erbitux, Tarceva and Alimta – higher than the US by 2013
- Mixed picture in terms of the correlation between NICE/HAS recommendations and sales in the UK/France
- French uptake sometimes takes off in advance of HAS decisions

# Sales data: UK

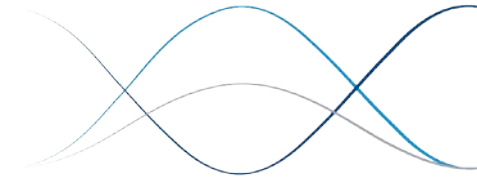


- We observe upward inflexions in sales at the time of positive (albeit restricted) NICE recommendations (e.g. Alimta)
- We observe increases in sales after the introduction of the Cancer Drugs Fund in 2010 (e.g. Avastin)

## Sales of Alimta (left) and Avastin (right) in the UK compared with EMA authorisations and NICE decisions

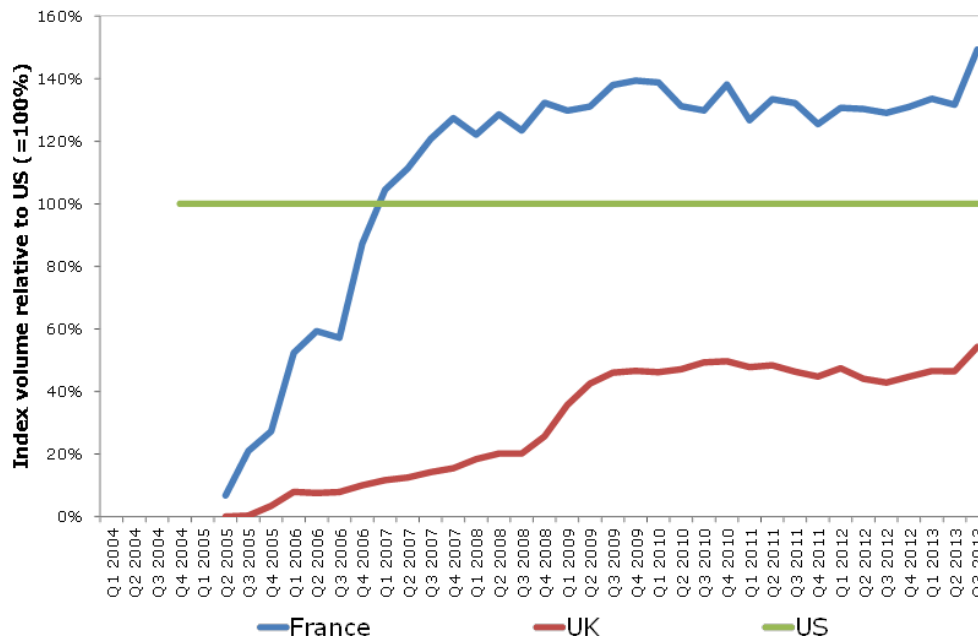


# Usage patterns



- Unsurprisingly, there is a *prima facie* link between expansions in licensed indications and changes in sales
- We observe strong growth in use as the first post-launch label expansions occur, followed by a flattening or reduction in usage
- Could be due to competition or changes in treatment patterns

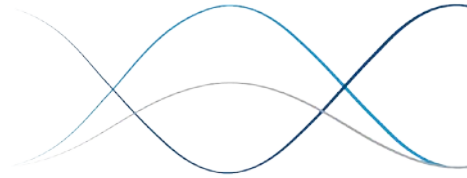
## Tarceva volume usage mg per 100,000 population – France, UK and US





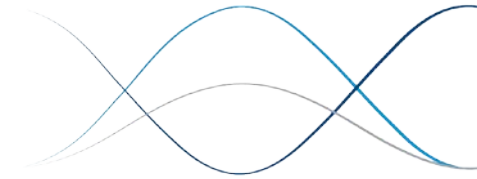
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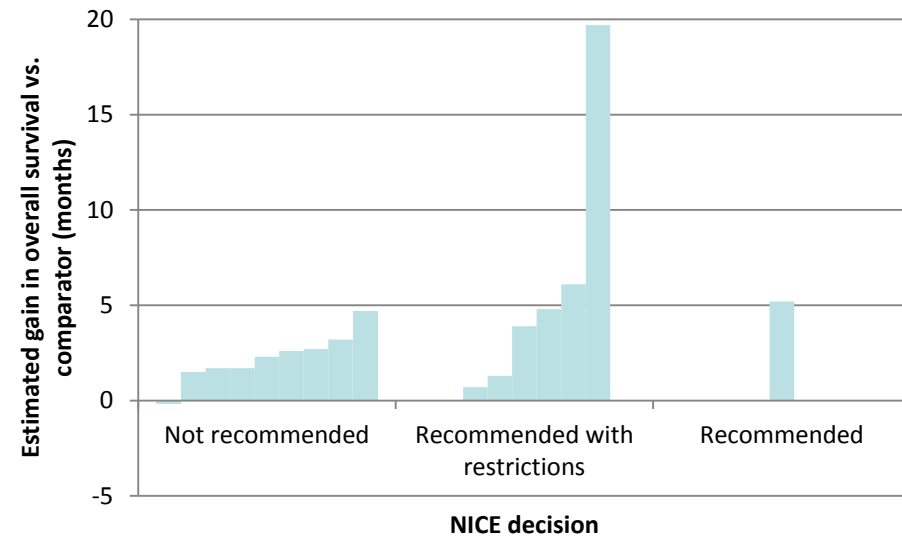
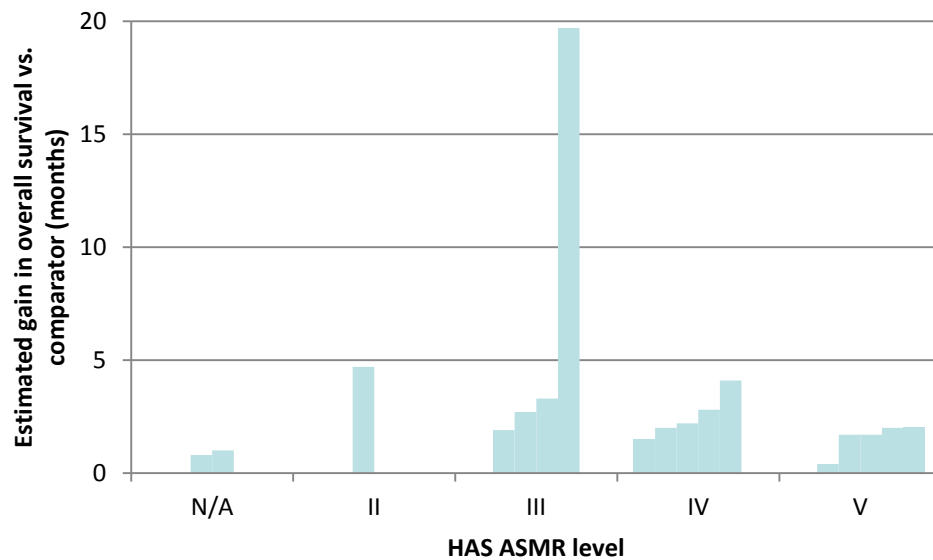


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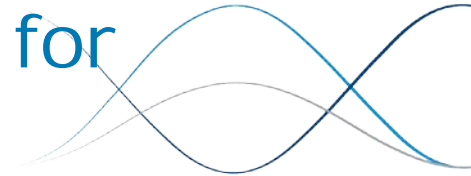
# Recognition of the value of health outcome improvements



- Results for both HAS and NICE seem to suggest a positive association between gains in overall survival and recommendation decision
- However, we know that NICE's decision-making is guided by several factors beyond cost-effectiveness alone, such as considerations about equity or the severity of the underlying illness
- Mauskopf et al. (2013) report that budget impact did not predict overall recommendations by NICE but was certainly associated with the application of restrictions on its recommendations

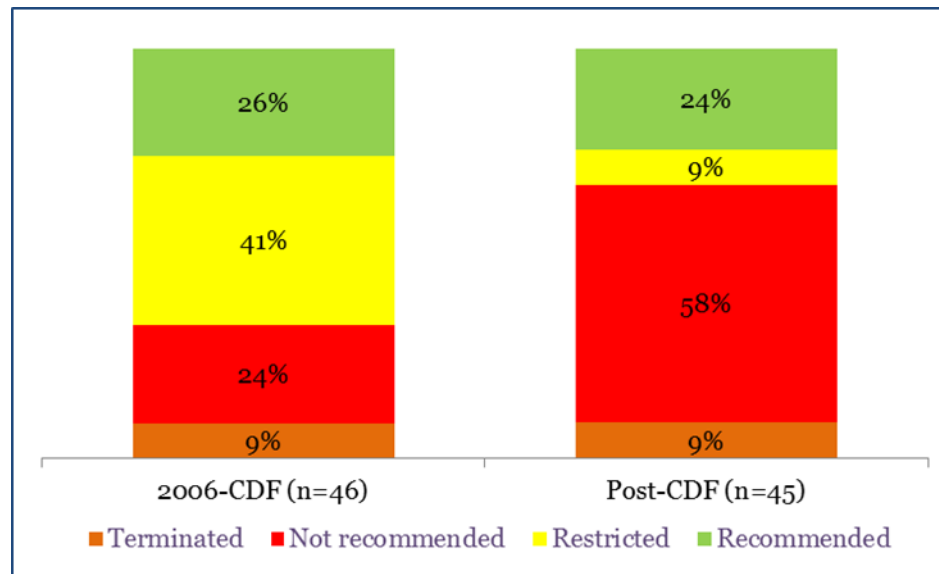


# Appropriateness of the methods for appraising oncology treatments



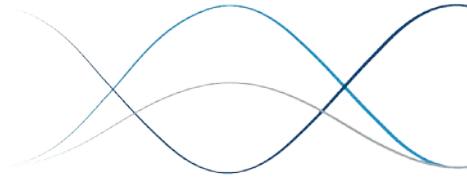
- NICE is much more likely than HAS not to recommend the use of a given oncology product
- One interpretation of the introduction of the CDF in England is that the standard NICE approach, which compares the ICER of the drug under appraisal with a cost-effectiveness threshold, is not always appropriate for oncology treatments

## Trends in NICE decisions for oncology drugs pre- and post-CDF



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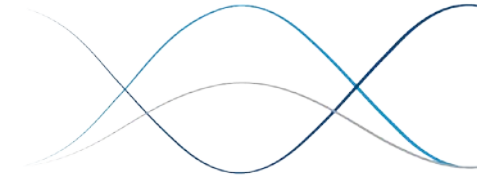
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# Conclusions

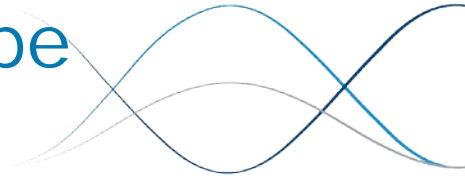
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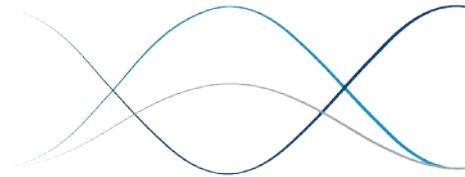
- We demonstrate the need for health systems and policy makers to consider how product life-cycle considerations affect the value of medicines, and in particular, oncology medicines
- Since HTA processes for branded, innovative medicines generally aim to give greater rewards to more significant innovations, it is important to understand that the innovativeness can be demonstrated in terms of the ways in which a product's value expands across over time

# Research questions that should be developed further

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- The question of whether HTA systems based on both clinical and cost-effectiveness should treat oncology treatments differently from non-oncology treatments
- The question of whether — and if so, how — HTA processes should take into account explicitly the issue of path dependency (i.e. temporal interdependencies among indications) when assessing new medicines at launch
- The question of whether and how pricing and reimbursement systems should move away from “one price across all indications” to more “flexible pricing” approaches
- The question of what factors drive uptake of medicines in practice
- The question of the extent to which the issues identified for oncology treatments — value expansions, path dependency, and multiple indications — are also applicable to non-oncology treatments



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To enquire about additional information and analyses, please contact Dr. Jorge Mestre-Ferrandiz at [jmestre-ferrandiz@ohe.org](mailto:jmestre-ferrandiz@ohe.org)

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