Background

- The Cancer Drugs Fund (CDF) in England has an annual budget of £280 million to fund cancer drugs on the NHS that have either not been assessed or have been rejected by the National Institute for Health and Care Excellence (NICE).1
- Due to increasing expenditure (estimated at £390 million at November 2014) the CDF revised its process for evaluating drugs to include an assessment of cost (the median drug cost per patient).
- In December 2014, drugs currently funded by the CDF were re-assessed based on the additional criteria and 16 (across 25 indications) were removed from the list.
- Previous analysis on a subset of the drugs that were re-assessed indicated that drugs with a higher budget impact may be more likely to be rejected by the CDF.2
- Recently in May 2015, select drugs on the CDF were again re-evaluated and a further 4 were removed.

Objectives

- We aimed to expand the previous analysis to all indications re-appraised by the CDF from December 2014 to May 2015, to investigate whether the trend of rejection for drugs with a larger budget impact holds when a larger sample size is used.

Methods

- The cost per cycle, cycle length and median duration of treatment were extracted from the CDF decision summaries and the average cost per patient was calculated for drugs re-assessed between December 2014 and May 2015.
  - In total, 45 decision summaries referred to treatments available on the CDF list and were included in our analysis.
- The budget impact of those drugs that had previously been reimbursed by the CDF was calculated based on the number of notifications that the CDF received in 2014.
- A point-biserial correlation coefficient ($r_p$) was used to assess whether cost per patient and total budget impact were correlated with the CDF reimbursement decision.
- Clinical scores were also extracted from the CDF decision summaries and analysed alongside the cost per patient and budget impact variables.
  - The total clinical score was a composite of individual scores for Progression Free Survival (PFS), Overall Survival (OS), Quality of Life (QoL), Toxicity and Unmet Need.
- A logistic regression model was developed in R to explore the impact of these parameters on the CDF decision to remove or retain drugs from the list. An optimisation procedure using backward elimination from the full model was carried-out using the Akaike information criterion (AIC).

Table 1. Summary of logistic regression outputs and optimisation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>p-value</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Null Model Intercept</td>
<td>-0.511</td>
<td>0.327</td>
<td>0.118</td>
<td>54.925</td>
</tr>
<tr>
<td>Full Model Intercept</td>
<td>-3.589</td>
<td>1.032</td>
<td>&lt;0.001*</td>
<td>37.495</td>
</tr>
<tr>
<td>Clinical Score</td>
<td>0.321</td>
<td>0.248</td>
<td>0.035*</td>
<td></td>
</tr>
<tr>
<td>Cost per Patient</td>
<td>-6.98x10^-6</td>
<td>3.80x10^-6</td>
<td>0.035*</td>
<td></td>
</tr>
<tr>
<td>Budget Impact</td>
<td>-3.80x10^-6</td>
<td>4.32x10^-6</td>
<td>0.381</td>
<td></td>
</tr>
<tr>
<td>Optimised Model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-3.662</td>
<td>1.037</td>
<td>&lt;0.001*</td>
<td>36.708</td>
</tr>
<tr>
<td>Clinical Score</td>
<td>0.513</td>
<td>0.240</td>
<td>0.032*</td>
<td></td>
</tr>
<tr>
<td>Cost per Patient</td>
<td>5.88x10^-5</td>
<td>2.88x10^-5</td>
<td>0.035*</td>
<td></td>
</tr>
</tbody>
</table>

Results

Investigation of the larger sample set confirmed the initial results of the previous analysis and determined that there was a positive correlation between the cost per patient and the probability of inclusion in the CDF ($r_p=0.643$; Figure 1).
- However, when investigating the larger sample size, the budget impact was found to have little influence on the CDF reimbursement decision ($r_p=0.105$; Figure 2).
- Based on the optimised model, the logistic regression analysis confirmed that the cost per patient was a significant predictor of whether a drug was removed or retained on the CDF list and was associated with a positive coefficient ($β=5.88x10^-6$, p=0.039; Table 1).
  - Similarly, in this model the clinical score was also found to be statistically significant (p=0.032; Table 1); however, the components of this parameter did not reach significance when tested individually.
- Incorporation of the budget impact parameter in the logistic regression model did not improve the model fit although this did indicate that a larger budget impact may be associated with a lower probability of being accepted; however, this relationship was not found to be significant ($β=-3.78x10^-6$, p=0.381, Table 1).
- Based on the optimised model, an increase in the median cost per patient of £1,000 resulted in a 6% increase in the odds of a positive CDF decision.
  - The predicted probability of a positive CDF decision with increasing costs (at a mean clinical score) is presented in Figure 3.
- The positive association between the cost per patient and the probability of being accepted is likely due to more favourable clinical evidence. This is demonstrated by the association between this variable and the key clinical parameters; Cost per patient was moderately correlated with PFS ($r_p=0.58$) – Cost per patient was weak-to-moderately correlated with OS ($r_p=0.3$).
- The Clinical Score afforded to each drug appraised by the CDF remained the most impactful predictor of approval, with a unit change of 1 resulting in a 67% increase in the odds of being approved.

Discussion

- Based on the updated analysis presented, it was apparent that the budget impact of drugs appraised for approval by the CDF does not influence decision making.
- However, based on the increased data set, the positive correlation associated with cost per patient remained, and logistic regression analysis confirmed this parameter as a statistically significant predictor of approval on the CDF.
- Despite the counter-intuitive nature of this result, this can largely be explained by the positive association between the cost of treatment and the clinical outcomes of the patient.
- The main limitation of our analysis was that the budget impact was calculated solely based on the notifications that the CDF received in 2014; this means that there is incomplete data for drugs that became available in 2014 or later, and that the true population may have been underestimated in cases where clinicians are not requesting use of drugs from the CDF.
- Additionally, in instances where the median duration of treatment was unavailable, PFS was used as a proxy measure, in line with assumptions applied by the CDF Committee.

Conclusions

- Although the CDF’s new criteria for reimbursement do involve an evaluation of the cost of each drug, it seems that neither the cost per patient nor the overall budget impact greatly influence their decisions.
- The total score based on the clinical evidence of the drug under consideration remains the most important determinant of whether a drug will be approved or not.

References