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Economic Implications of Instituting Clinical Care Pathways in Metastatic Colorectal Cancer

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BACKGROUND

- In an effort to improve quality of oncology care and reduce costs, payers have introduced cancer treatment pathways that are guideline-recommended treatment protocols for specific patient presentations and are chosen based on efficacy, toxicities, and costs.
- Though pathways intend to control costs by reducing variation in treatment patterns, the net impact of pathways on cost of care is not clear given the additional costs associated with pathway initiation and administration, including reimbursement incentives to clinicians who treat patients with on-pathway regimens.
- In metastatic colorectal cancer (mCRC), treatment options historically have included combination chemotherapy regimens, such as leucovorin, fluorouracil, and irinotecan (FOLFIRI), and leucovorin, fluorouracil and oxaliplatin (FOLFOX).
- More recently, biologic agents such as the VEGF-A inhibitor Avastin (bevacizumab), and the EGFR inhibitors Erbitux (cetuximab) and Vectibix (panitumumab) have also been included in treatment options.
- The choice of biologic can be difficult, given contradictory findings regarding efficacy between trials.
- Often, this treatment choice is determined by cost alone, and thus, some pathways have been designed to include panitumumab and exclude cetuximab, given acquisition costs at indicated dosing.

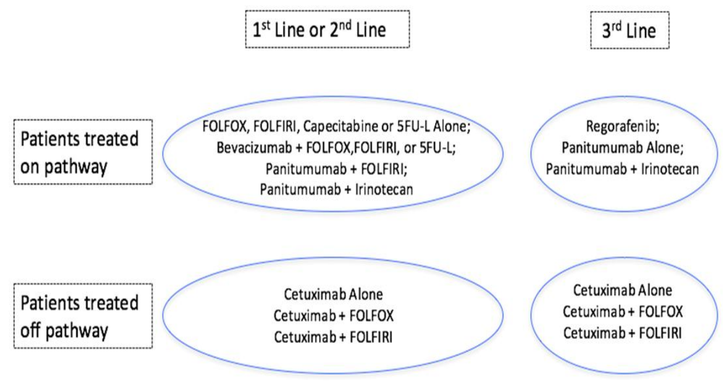
OBJECTIVE

- The objective of this study was to compare the financial impact of a scenario in which treatment pathways for mCRC were implemented versus an alternative scenario without pathways. The specific pathway program modeled consisted of incentives to clinicians for using specific treatment regimens, including panitumumab but excluding cetuximab, among patients with mCRC.

METHODS

- An economic model was built to estimate and compare the costs to US payers of treating KRAS wild-type (WT) mCRC patients with pathway implementation versus without pathway implementation.
- On-pathway regimens for each line of therapy are shown in the top row of the Figure 1 and included panitumumab. Off-pathway regimens were cetuximab-based.

Figure 1. Treatment Regimens for Patients Treated on Pathway versus off Pathway in Pathway Implementation Scenario



5FU-L: Leucovorin + Fluorouracil.

MODEL POPULATION

- The model population was defined as adult mCRC patients with KRAS WT, EGFR-expressing tumors.
- We estimated the number of patients fitting this criteria by line of therapy by funneling down from a hypothetical 1 million member plan (Table 1).

Table 1. Eligible Patient Population[a]

	%	N	Source
Plan size	-	1,000,000	Assumption
Incidence of colorectal cancer	0.04%	424	SEER 2015
Proportion metastatic	20%	85	SEER 2015
Proportion KRAS WT	63%	53	Van Cutsem, 2011
Proportion on 1st line treatment	63%	34	BMS[b] Data on File
Proportion on 2nd line treatment	25%	14	BMS[b] Data on File
Proportion on 3rd line treatment	11%	6	BMS[b] Data on File

[a] Values are rounded
[b] BMS: Bristol-Myers Squibb

COSTS

Cost components included in the model

- Product acquisition & administration, including backbone & loading dose, applied for average duration of treatment from package inserts (PIs) (Table 2, Table 5)
- Genetic mutation testing (Table 3)
  - All first-line patients accrued KRAS and NRAS testing costs, estimated based on average list price of currently available tests.
- Pathway program initiation, administration, and incentive fees (Pathway scenario only) (Table 3).
  - One-time initiation cost assumes 12 clinicians involved in developing pathway over 2 days (16 hours) of meetings, using hourly wage of $93.74.
  - Administration assumes 20 minutes per claim and wage rate for physician.
  - Incentive amount and timing based on an existing pathway.
- Adverse event treatment (Table 3)

Table 2. Product Costs

Product	Total Product Costs per Treatment Cycle[a,b]
Cetuximab	
Loading Dose	$4,329
Subsequent Dose	$3,156
Panitumumab	$5,651
Bevacizumab	
with FOLFIRI or alone	$3,281
with FOLFOX	$5,363
Regorafenib	$12,497
FOLFOX	$2,668
FOLFIRI	$2,394
5FU-L	$1,967
Irinotecan	$2,688
Capecitabine	$2,429
Best Supportive Care[c]	$4,444

[a] Total product costs include acquisition and administration costs for each product.
[b] Acquisition costs based on PriceRx as of August 2015. Administration cost based on Physicians Fee and Coding Guide 2015. Assumes dosing schedule described in product package inserts (PIs), average patient body surface area of 1.7 m^2, and average body weight of 70 kg.
[c] Cost per dose reflects daily cost and cost per treatment cycle represents monthly cost.

Table 3. Costs of Other Components

Cost Component	Value	Source
Genetic testing cost per patient	$1,243	Dedham Group Primary and Secondary Research 2015
Pathway implementation costs		
Program initiation	$17,998	Feinberg 2012; US Bureau Labor Statistics 2015
Program administration per claim	$31.25	Epling 2014; US Bureau Labor Statistics 2015
Monthly incentives		
Payment per month	$350	WellPoint 2015
Maximum months	6	WellPoint 2015
Adverse event treatment cost per event[a,b,c]	$4,814 - $9,520	Burudpakdee 2012

[a] Grades 3-4 events only; adverse events were selected if they occurred in greater than 5% of patients in at least one product or regimen included in this analysis, and incurred significant treatment costs.
[b] Rates derived from prescribing information for each product. When data was not available, rates were also abstracted from published literature. When multiple event rates were available from more than one source, an average of all rates was taken for each regimen.
[c] Costs reported in 2014 US$.

PRODUCT DOSING & TREATMENT DURATION

- Real-world data indicates that not all cetuximab patients receive the indicated loading dose, and some patients get injections once every two weeks as opposed to indicated weekly injections (Table 4).
- NCCN guidelines also include every other week dosing of cetuximab.

Table 4. Cetuximab Dosing

Parameter	Value	Source
% patients receiving loading dose	64%	BMS[b] data on file
% patients with 1 injection every 2 weeks[a]	39%	BMS[b] data on file

[a] All others receive 1 injection weekly.
BMS: Bristol-Myers Squibb

Table 5. Average Duration of Treatment

Line of Therapy	Average Treatment Duration (months)[a]
1st line	6.3
2nd line	4.6
3rd line	4.6

[a] Values based on averages from prescribing information for all products.

PRODUCT UTILIZATION: WITH VS. WITHOUT PATHWAY IMPLEMENTATION

- With pathway implementation, a 10% shift of patients from cetuximab- to panitumumab-containing regimens is assumed across first-, second-, and third-line therapy.
  - This shift reduces cetuximab utilization from −13% of the entire population to −3%.
  - Shifted first-line cetuximab patients are distributed between panitumumab-containing regimens based on the No Pathway panitumumab proportions in each regimen.
- Utilization of all other regimens remains constant between the Pathway and No Pathway implementation (Table 6).
- The proportion of patients on each regimen was multiplied by the number of patients in the model to estimate the number of patients on each regimen (Table 7).

Table 6. Likelihood of Treatment[a]

	No Pathway Implementation			With Pathway Implementation[b]		
	1st Line	2nd Line	3rd Line	1st Line	2nd Line	3rd Line
Panitumumab +						
Alone	1.0%	2.3%	3.4%	3.7%	9.4%	18.2%
Irinotecan	0.4%	0.0%	0.7%	1.5%	0.0%	3.6%
FOLFIRI	0.5%	2.8%	1.4%	1.9%	11.7%	7.3%
All Panitumumab	2.0%	5.1%	5.5%	7.1%	21.1%	29.1%
Cetuximab +						
Alone	1.7%	5.4%	7.6%	0.4%	1.4%	1.9%
FOLFIRI	4.3%	14.7%	22.8%	1.1%	3.8%	5.8%
FOLFOX	0.8%	1.4%	1.4%	0.2%	0.4%	0.4%
All Cetuximab	6.9%	21.5%	31.7%	1.8%	5.5%	8.1%
Chemotherapy Alone						
FOLFIRI	2.3%	7.1%	5.5%	2.3%	7.1%	5.5%
FOLFOX	14.2%	4.2%	5.5%	14.2%	4.2%	5.5%
5FU-L	3.7%	2.3%	1.4%	3.7%	2.3%	1.4%
Capecitabine	0.2%	3.1%	2.8%	0.2%	3.1%	2.8%
All Chemo Alone	20.4%	16.7%	15.2%	20.4%	16.7%	15.2%
Bevacizumab +						
Alone	9.5%	3.1%	4.9%	9.5%	3.1%	4.9%
FOLFIRI	18.4%	31.4%	17.9%	18.4%	31.4%	17.9%
FOLFOX	35.0%	10.5%	13.1%	35.0%	10.5%	13.1%
5FU-L	3.7%	5.7%	4.1%	3.7%	5.7%	4.1%
All Bevacizumab	66.6%	50.6%	40.0%	66.6%	50.6%	40.0%
Regorafenib Alone	0.1%	1.1%	0.7%	0.1%	1.1%	0.7%
Best Supportive Care	4.1%	5.1%	6.8%	4.1%	5.1%	6.8%

[a] Bristol-Myers Squibb Market Data 2015.
[b] Default shift in utilization from cetuximab to panitumumab with pathway implementation sums to 10% of the entire model population (1st, 2nd, and 3rd lines), based on data from Hoverman JOP 2014.

Table 7. Patients per Regimen by Line of Therapy

	No Pathway Implementation			With Pathway Implementation		
	1st Line	2nd Line	3rd Line	1st Line	2nd Line	3rd Line
Panitumumab +						
Alone	0.3	0.3	0.2	1.3	1.3	1.1
Irinotecan	0.1	0.0	0.0	0.5	0.0	0.2
FOLFIRI	0.2	0.4	0.1	0.6	1.6	0.4
All Panitumumab	**0.7**	**0.7**	**0.3**	**2.4**	**2.9**	**1.8**
Cetuximab +						
Alone	0.6	0.7	0.5	0.2	0.2	0.1
FOLFIRI	1.5	2.0	1.4	0.4	0.5	0.4
FOLFOX	0.3	0.2	0.1	0.1	0.0	0.0
All Cetuximab	**2.3**	**2.9**	**1.9**	**0.6**	**0.7**	**0.5**
Chemotherapy Alone						
FOLFIRI	0.8	1.0	0.3	0.8	1.0	0.3
FOLFOX	4.8	0.6	0.3	4.8	0.6	0.3
5FU-L	1.2	0.3	0.1	1.2	0.3	0.1
Capecitabine	0.1	0.4	0.2	0.1	0.4	0.2
All Chemo Alone	**6.9**	**2.3**	**0.9**	**6.9**	**2.3**	**0.9**
Bevacizumab +						
Alone	3.2	0.4	0.3	3.2	0.4	0.3
FOLFIRI	6.2	4.3	1.1	6.2	4.3	1.1
FOLFOX	11.8	1.4	0.8	11.8	1.4	0.8
5FU-L	1.2	0.8	0.3	1.2	0.8	0.3
All Bevacizumab	**22.5**	**6.9**	**2.4**	**22.5**	**6.9**	**2.4**
Regorafenib Alone	**0.0**	**0.2**	**0.0**	**0.0**	**0.2**	**0.0**
Best Supportive Care	**1.4**	**0.7**	**0.4**	**1.4**	**0.7**	**0.4**
Total Patients	**33.7**	**13.6**	**6.1**	**33.7**	**13.6**	**6.1**

RESULTS

Annual Costs And Per-Member Per-Month (PMPM) Costs: With Vs. Without Pathway Implementation

- Costs with and without pathway implementation are shown in Table 8 and Figure 2.
- We found that implementation of pathways increased total costs to the plan by $78,956.

Table 8: Annual Costs by Component and PMPM

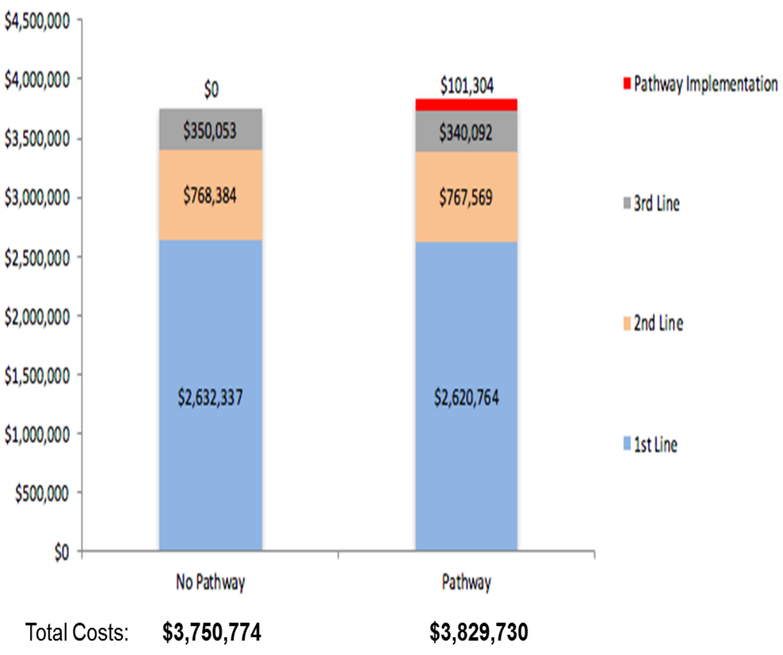
Comparator	Product Costs		Adverse Event	Genetic Testing	Pathway Related	Total Annual	PMPM
	Acquisition	Administration					
No Pathway	$2,220,539	$1,319,102	$169,188	$41,945	$0	**$3,750,774**	**$0.3126**
Pathway	$2,263,429	$1,259,093	$163,959	$41,945	$101,304	**$3,829,730**	**$0.3191**
Difference[a]	$42,890	-$60,009	-$5,229	$0	$101,304	**$78,956**	**$0.0066**

[a] Difference reflects additional costs with pathways vs. without pathways, such as a negative number reflects a cost savings with pathways.

RESULTS (CONTINUED)

Annual Costs: With vs. Without Pathway Implementation

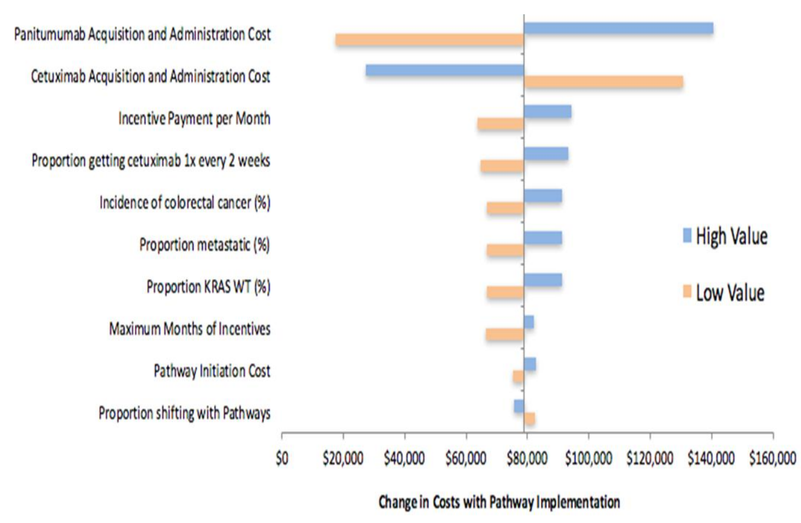
Figure 2. Annual Costs by Line of Treatment: With vs. Without Pathway Implementation



Sensitivity Analyses

- In sensitivity analyses, the value of each parameter was varied by +/- 20% of the base case value.
- The parameters with the largest impact included the acquisition and administration costs of panitumumab and cetuximab, as well costs of implementing pathways (Figure 3).
- Other parameters, such as the cost of adverse event treatment and genetic testing, were found to have minimal impact.

Figure 3. Sensitivity Analysis Tornado Diagram



EXECUTIVE SUMMARY

- In a model with a 1 million-member plan size, 53 patients are estimated to receive treatment for KRAS WT mCRC.
- The model predicts that with a mCRC pathway implementation, cost to payers will increase by $0.0066 PMPM, or approximately $79,000 annually.
- With pathway implementation:
  - Product acquisition and pathway related costs were estimated to increase by $42,890 and $101,304, respectively, compared to without pathway implementation.
  - Product administration and adverse event treatment costs were estimated to decrease by $60,009 and $5,229, respectively, compared to without pathway implementation.

LIMITATIONS

- In this study, we only assessed the cost differences with implementation of the pathway without taking into consideration clinical outcomes.
- There are specific features of the modeled incentive program that may vary in practice and impact the generalizability of results. For example, we assumed that clinician reimbursement would increase by $350 per month for a maximum of 6 months for each patient treated with an on-pathway regimen, based on the WellPoint pathway. If the specific incentive amount or maximum duration were varied, the estimated cost increase with pathway implementation would also change.
- The assumption that 10% of patients would switch from cetuximab-based regimens to panitumumab-based regimens with the implementation of pathway was from a published study assessing breast, lung and colorectal cancer patients from a limited sample of facilities in Texas (Hoverman 2014). Whether this figure is generalizable is uncertain, although sensitivity analyses showed that this parameter was not as influential as others.
- There was no single trial that reported adverse event rates for all regimens, therefore, data had to be combined from multiple sources. However, care was taken to ensure that the estimates came from reliable sources such as pivotal trials considered in drug approval process, and in sensitivity analyses, these parameters had a negligible impact on model results.

CONCLUSIONS

- Implementation of clinical care pathways may lower the cost of care by reducing variability in treatment; however, there are additional costs associated with the set-up and implementation of the pathway.
- In mCRC, assessment of real world utilization of panitumumab and cetuximab, as well as inclusion of the upfront and variable costs of implementing a pathways program, indicates that pathways that discourage cetuximab use can actually increase overall plan costs.
- Decision makers concerned about healthcare costs in oncology should consider all relevant costs, inclusive of incentives and administration, when attempting to implement cost-saving measures.

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