Validating costing methodologies used in the health economic literature of colorectal cancer

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1. Introduction

In 2018, nearly half a million new cases of colorectal cancer were diagnosed in Europe alone. Moreover, almost a quarter of a million deaths were attributed to it, making colorectal cancer the second most deadly cancer in Europe (WHO, 2018). The cumulative risk of contracting colorectal cancer is over 1 percentage point higher for men than it is for women (WHO, 2018) with the overall incidence rate predicted to rise considerably over the coming years (European Commission, 2017). The cost burden of colorectal cancer, which has already risen significantly over time, is therefore forecast to dramatically increase, with not only higher incidence rates, but an ageing population, rising long-term survival and costly medical technology advances too (Ó Céilleachair et al, 2013).

The increasing cost burden means that it is essential now more than ever to accurately assess the costs of all stages of the colorectal cancer pathway, from diagnosis to treatment and longer-term follow up. Accurate and consistent costing methodologies are fundamental in ensuring that the full burden of colorectal cancer on healthcare providers, government, and individuals is realised. Furthermore, effective costing analysis is crucial for performing precise economic evaluations and making valid and meaningful comparisons between procedures.

Examining the heterogeneity across costing methodologies is essential for creating a framework that future work can use to ensure methodological homogeneity, thus increasing comparability across studies and enabling generalisations to be made from results. The motivation for this study stems from a recent literature review by Špacírova et al (2020). In their paper, Špacírova and colleagues examine 21 recent economic evaluations and review the costing approaches implemented in terms of the description given, the data and assumptions made and the level of accuracy and precision required for the economic evaluation. At the outset, Špacírova et al (2020) outline clear costing methodology standards and use these in their assessment of the extent to which their selection of publications align to these standards. Overall, they find that there are substantial inconsistencies across the literature and they propose that future health economic studies use their standard classification when describing their costing methodology.

This study's objective is to determine how closely the health economic literature in the colorectal cancer specific context follows the standard classification as outlined in Špacírova et al (2020). To achieve this aim, we review 20 recent colorectal cancer health economic studies, covering both economic evaluation and cost of illness studies. There are three main ways to classify economic evaluations: cost-effectiveness, cost-utility and cost-benefit analysis. Evaluations address a specified research question by comparing the costs and outcomes of an intervention compared to alternatives. By contrast, cost of illness studies measure the burden of illness overall in monetary terms.

To determine how closely the studies we identified follow the standard classification as set out in Špacírova et al (2020), we firstly establish how frequently the health economics literature of colorectal cancer uses the key terms. Secondly, we discuss how the literature uses the key costing components required in order to identify which approach is used to value resource use

items. Similarly, we discuss how the literature uses the key components required in order to establish the level of accuracy in the identification of the cost components.

The structure of this paper is as follows. First, our identification methodology is discussed and details of each costing approach described. We then present the results of our literature review and analyse the adherence of each paper to the Špacírova et al (2020) descriptions of costing methodology, using the three steps described above. Lastly, we discuss several steps that future studies could take in order to improve transparency in reporting costing methodologies and reduce heterogeneity in costing approaches.

2. Methodology

The literature examined in this study provide a cross-sectional overview of the most recent health economics literature on colorectal cancer. The publications examined come directly from a recent systematic review of colorectal cancer health economic studies (Lemmon et al, 2020). The publications in that review were scoped from OVID Medline with the specification of being European, English language papers published between 2009 and 2019.

From the 37 included studies, a representative sample of 20 papers consisting of a mixture of cost of illness studies and economic evaluations were used in this study. They cover a broad spectrum of different perspectives, phases of care and types of study were reviewed to ensure that the conclusions drawn and solutions offered generalize to the colorectal cancer literature as a whole. The cross-section covers literature from nine different healthcare systems in Europe (UK n = 10; France n = 2; Italy n = 2; Ireland n = 1; Switzerland n = 1; Belgium n = 1; Spain n = 1; Greece n = 1)[1]. From the 20 studies examined, exactly half are cost of illness studies and half are economic evaluations.

As outlined previously, we followed Špacírova et al (2020) costing methodology standards when reviewing the costing approaches of the selected studies. The key identification features of each type of methodology are shown in Figure 1.

The terms gross costing and micro costing are used to describe the level of accuracy in the identification of the cost components. Gross costing uses aggregated cost data, and therefore has less identification accuracy in its costing approach compared to micro costing. Micro costing does not use aggregate data and instead defines costs at an extremely detailed level, usually in the form of a comprehensive table of unit costs, resulting in a more accurate identification of costs (Tan et al, 2009).

The use of a top-down or bottom-up costing approach determines the valuation accuracy of the cost components. A bottom-up approach is often regarded as the most accurate in terms of valuation accuracy (Tan, 2009). This is because resource use is valued at the patient level, thus creating patient specific unit costs. Top-down costing uses organisational level aggregated costs that are divided between patients to get an average resource use cost per patient. It is argued that this costing approach yields cost valuations that are less accurate (Tan et al, 2009).

[1] Several papers specify England, rather than the UK, however for the purposes of this review these will be treated as the same country and healthcare system.

Figure 1: Key Features of Costing Approaches

COSTING APPROACH	**KEY FEATURES**
Micro-costing	• Resource use identified at a detailed level • A specified unit cost table or appendix • High levels of costing accuracy • E.g. dosage costs for medication
Gross-costing	• Resource use identified at an aggregated level • Patients and/or treatment costs grouped together • Lower levels of costing accuracy • E.g. total cost for whole treatment
Top-down	• Resource use allocated at an organisation level then divided down • Average costs per patient • E.g. Hospital department expenses divided by number of patients
Bottom-up	• Resource use identified at a patient level • Patient specific unit costs • E.g. individual treatment costs plus number of nights in hospital costs

From these definitions, we can combine the costing approaches to create a costing methodology, which can be seen in Figure 2. For example, bottom-up micro costing uses extremely detailed resource use data and values these resources at a patient level.

As discussed in Špacírova et al (2020), it can be extremely hard to distinguish costing approaches from one another. This is primarily due to identification and valuation of resources level of detail being a matter of personal preference (Špacírova et al, 2020). Moreover, studies often do not specify the costing methodology used and are regularly unclear when specifying their cost sources, cost types and approaches. Due to the ambiguity of the various costing methodologies, Špacírova et al (2020) find that the overlap between the types makes it difficult to definitively categorise methodologies.

Figure 2: Costing Methodology Matrix, Adapted from Tan et al, (2009)

	- Identification Accuracy +	
+ Valuation Accuracy -	Top-down gross costing	Top-down micro costing
+	Bottom-up gross costing	Bottom-up micro costing

We used a three-step process to determine how closely the health economic literature of colorectal cancer follows the costing methodologies as outlined in Špacírova et al (2020). This three-step approach is as follows:

1. We searched the papers to identify where the terms top-up and bottom-down, micro and gross costing were used
2. We checked how detailed the literature was in terms of describing the cost components i.e. was a micro or gross costing approach used
3. We identified whether or not papers were explicit in terms of how resource use items were valued i.e. was a top-down or bottom-up approach used

3. Results

3.1 Summary of the literature

Tables 1 and 2 in the Appendix respectively show summaries of the economic evaluation and cost of illness studies. Several key distinctions can be seen between the ways in which each type of study is conducted. Economic evaluations tended to specify the perspective in which the analysis is taken form, whilst only two of the cost of illness studies examined specified the study's perspective. Perspective is generally from either taken from a healthcare provider, societal or health insurance view, with the most common perspective seen being healthcare provider (n = 14). The perspective of the study determines the costs that are relevant and hence should be included. It is therefore crucial to ascertain the perspective (Mayer et al, 2017). For example, a study which specifies a social perspective should consider both the direct and indirect in the analysis, trying to encompass all the costs borne.

Similarly, where studies lasted for over one year most of the economic evaluations used an appropriate level of discounting to adjust the value of costs and benefits over time and account for future costs and benefits being valued less. Attema et al (2018) discusses how most economic evaluations of healthcare require cost discounting to take into account the intertemporal element of the intervention. NICE guidelines recommend that both costs and health outcomes should be discounted at a rate of 3.5% in order to achieve this (YHEC, 2016). However, the majority of cost of illness studies do not use discounting when it was appropriate to do so.

The type of costs used in the studies are also displayed in Tables 1 and 2. Costs are split into two types: direct and indirect costs. Direct costs are derived solely from the health intervention or phase of care being examined and are made up of direct medical costs and direct non-medical costs. The cost of the medications used to treat colorectal cancer, the cost of instruments used in surgery and the cost of hospital stays are all examples of direct costs. Indirect costs are derived from productivity, wages and patient utility lost as a result of the treatment or phase of care they are undergoing. Lost wages as a result of incapacitation or as a result of caring for a sick relative, time lost due to hospital visits and travel time are all examples of indirect costs. They are however, much harder to value than direct costs due to using opportunity cost to value lost time and productivity. Opportunity cost is a subjective measure as it depends on the unique preferences of the individual so spending a week in hospital has a different value depending on the busyness of the individual, their job etc.

Nineteen of the papers examined use direct costs in their costing methodology, with three of these papers also using indirect costs. One paper solely used indirect costs in its analysis. From the studies examined, ten were explicit in stating the types of cost used and ten were not, with the majority that were explicit (n = 8) being cost of illness studies.

In general, it was easy to identify the types of costs used in the studies, with the easiest identification of costs coming from the following studies. Francisci et al (2013), Bending et al (2010) and Lansdorp-Vogelaar at al (2018) demonstrate complete transparency in cost types, with each study explicitly stating the type used. Francisci et al (2013) and Bending et al (2010) do this in their introductions stating that their respective aims were to estimate direct costs. Bending et al (2010) plainly states the cost components that are included, which further shows clarity in the costing type through language used. Lansdorp-Vogelaar et al (2018) explicitly state in a 'costs' section that they will be using direct costs alongside patient time costs. In addition to the statements, the specification that a "modified societal perspective" is being used implies that indirect costs will also be included.

Jean-Claude et al (2012), Hanly et al (2013) and Halligan et al (2014) are not explicit in stating their cost types. Nevertheless, their description of costs and the language used make the cost type clear. Hanly et al (2013) is especially transparent and clear in their language use; stating firstly that the study is from a societal perspective, indicating indirect costs, and secondly by describing in detail how the costs components were derived, showing that only indirect costs such as time and lost wages were used.

The key elements needed to easily, and correctly identify the cost type used are therefore clarity in terms of language and transparency in the costs used. However, obviously the most useful tool for identifying costing type is the explicit stating of costing type.

In what follows, we present the costing methodology results using the three step process outlined previously.

3.2 Use of terms top-up and bottom-down, micro and gross costing

From the selection of studies examined, only two make reference to the costing approaches as defined by Špacírova et al (2020): Hall et al (2014) and Rao et al (2018). Moreover, it is only Hall et al (2020) who state that a costing approach will be used. Specifically, they state that the "costing uses a mixture of (a) top down costing … and, (b) bottom-up costing)". Rao et al (2018) simply states that they are using estimates from a previous micro-costing study.

The key characteristic that determines whether a study uses gross or micro costing is the level of detail in the resource use items – are they costs highly identified? Similarly, top-down and bottom-up costing are segmented by examining the valuation accuracy of the costs – are there clear individual patient costs or have they been collated and then apportioned down?

3.3 Explicitness in describing resource use items

For the identification of micro costing, the clearest indication was a table of unit costs being present either in the main body of the text or appendix. Pilgrim et al (2017) has an extremely detailed table of unit costs within the model parameters table, which shows the costs for procedures, consultations, and medications, with the main source being NHS reference costs. Halligan et al (2015) also provides a detailed tables of unit costs for different medications and dosages, as well as for a range of diagnostic procedures. Both of these studies are good examples of micro-costing. Micro costing is the most popular costing approach from the studies examined and other studies that use this method include Bending et al (2010), Corral et al (2016), Giulani et al (2011), Rao et al (2018) and Matter-Walstra et al (2016).

Gross costing was more difficult than micro costing to identify. In particular, Francisci et al (2013) use lump sum payments to determine costs, these are aggregated costs and therefore

fit with the gross costing methodology. Here, individual level patient costs are not identified and the treatments are grouped together under the lump sum payment.

3.4 Explicitness in valuation of resource use items

From the definition of a top-down approach it is found that several papers meet the criteria, with Bending et al (2010) and Francisci et al (2013) providing the most clarity on this. Francisci et al (2013) use the Diagnosis-related group (DRG) system where the government pay a lump sum determined by the diagnosis and treatment of the patient. Compiled DRG costs are then used to make single average patient cost. They also describe the process of how single patient costs are computed, with this method matching the top-down costing approach. Bending et al (2010) also describe the process of mean costs being calculated from overall total costs, aligning with the top-down costing method. Other studies that display the characteristics of a top-down study, but not as clearly as Bending and Francisci are Bullement et al (2017), Laudicella et al (2016) and Macaffe et al (2011).

Corral et al (2016) and Michalopoulos et al (2013) are both explicit in their cost valuation using individual patient costs. Corral et al (2013) uses individual patient level data and gathers "information of each person … to determine the specific phase of care costs for each patient"; clearly demonstrating a bottom-up costing approach. Likewise, Michalopoulos et al (2013) collected cost details for each patient from their admission day to discharge day, including the possibility of any readmission, describing the process of cost collection in detail. Pil et al (2016), Matter-Walstra et al (2016), Halligan (2015) and Pilgrim et al (2009) all also display characteristics of bottom-up costing.

4. Discussion

Explicit terminology in regards to costing methodology has rarely been used in the papers examined, indicating perhaps either a lack of knowledge of the names of the different approaches or that the authors feel that they do not need to explicitly state the methodology in order for it to be clear. As discussed, several papers have made the costing approach taken clear through the use of language and transparency in computations, however many of the papers examined were identified to align with part of the costing methodology. Therefore, explicitly stating the costing approach is a highly useful tool for ascertaining costing methodology.

As previously discussed, it is hard to completely discern one costing methodology from the other. Laudicella et al (2016) is a prime example of this where it is stated that costs are aggregated suggesting a top-down approach, but then they go on to discuss patient-level costs in detail, implying bottom-up costing. Hall et al (2014) state that they use a mixture of both costing types, however upon examination it was found that more bottom-up costing methodology was used with patient records being linked to costs using the national PLICS scheme. Kearns et al (2014) use costs from another paper which is unclear about their costing approach and therefore it is uncertain what methodology they employ. Like top-down and bottom-up costing, gross and micro costing can be hard to untangle from one another. Also, as mentioned previously, due to Kearns et al (2014) taking its costs from another paper it is hard to distinguish whether the costing approach is gross or micro.

Micro and gross costing was, on the whole, easier to identify than the bottom-up and top-down. This was likely due to the accuracy of costs being more clearly stated and represented with the use of unit cost tables, whereas to determine top-down or bottom-up costing the computations used need to be clear.

Overall, the findings in the context of colorectal cancer literature echo those of Špacírova et al (2020). In particular, it was hard to distinguish costing methodologies exactly from one another as the studies do not directly adhere to the guidelines for each approach as set out in Špacírova et al (2020). Furthermore, we found a convergence between the costing methodologies, with the line between each end of the spectrum being a matter of subjective preference. This result coincides with Špacírova et al (2020): it is hard to definitively categorise costing methodologies.

Going forward, in order to improve transparency in the costing methodology used, studies should consider implementing a number of practices. Firstly, they should explicitly state whether they use micro, gross, top-down or bottom-up costing, providing clear evidence of how they do so. Next, to help discern between top-down and bottom-up costing, studies should provide clarity in their computations and clearly state cost sources. This would greatly improve the identification of the valuation accuracy. Lastly, to discern between gross and micro costing, the identification of costs used should be made clear. The simplest way to do this would be through the use of a unit costs table, as seen in some of the studies examined.

One suggestion for future research would be to develop a reporting standards checklists for health economics studies that carry out costing, similar to the CHEERS checklist. CHEERS is a tool used to ensure that all relevant items are included when reporting economic evaluations of health interventions and is an extremely useful reference tool for good reporting practices in health economics studies. A similar reporting standards checklist would be a useful tool in ensuring that costing methodologies are more homogeneous and allow for studies to be easily replicated and generalised.

5. References

Attema, A., Bleichrodt, H. and L'Haridon, O.,, 2018. Abiguity preferences for health. Health Economics, 27(11), pp.1699-1716.

Bending, M., Trueman, P., Lowson, K., Pilgrim, H., Tappenden, P., Chilcott, J. and Tappenden, J., 2010. Estimating the direct costs of bowel cancer services provided by the National Health Service in England. *International Journal of Technology Assessment in Health Care*, 26(4), pp.362-369.

Bullement, A., Underhill, S., Fougeray, R. and Hatswell, A., 2018. Cost-effectiveness of Trifluridine/tipiracil for Previously Treated Metastatic Colorectal Cancer in England and Wales. *Clinical Colorectal Cancer*, 17(1), pp.143-151.

Corral, J., Castells, X., Molins, E., Chiarello, P., Borras, J. and Cots, F., 2016. Long-term costs of colorectal cancer treatment in Spain. *BMC Health Services Research*, 16(1).

European Commission, 2020. *Cancer Screening In The European Union 2017*. [online] European Commission. Available at: <https://ec.europa.eu/health/sites/health/files/major_chronic_diseases/docs/2017_cancerscreening_2ndreportimplementation_en.pdf> [Accessed 25 August 2020].

Francisci, S., Guzzinati, S., Mezzetti, M., Crocetti, E., Giusti, F., Miccinesi, G., Paci, E., Angiolini, C. and Gigli, A., 2013. Cost profiles of colorectal cancer patients in Italy based on individual patterns of care. *BMC Cancer*, 13(1).

Giuliani, J., Indelli, M., Marzola, M., Raisi, E. and Frassoldati, A., 2012. The Management of Skin Toxicity during Cetuximab Treatment in Advanced Colorectal Cancer: How much does it Cost? A Retrospecive Economic Assessment from a Single-Center Experience. *Tumori Journal*, 98(4), pp.408-412.

Hall, P., Hamilton, P., Hulme, C., Meads, D., Jones, H., Newsham, A., Marti, J., Smith, A., Mason, H., Velikova, G., Ashley, L. and Wright, P., 2015. Costs of cancer care for use in economic evaluation: a UK analysis of patient-level routine health system data. *British Journal of Cancer*, 112(5), pp.948-956.

Halligan, S., Dadswell, E., Wooldrage, K., Wardle, J., von Wagner, C., Lilford, R., Yao, G., Zhu, S. and Atkin, W., 2015. Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicentre randomised trials with economic evaluation (the SIGGAR trials). *Health Technology Assessment*, 19(54), pp.1-134.

Hanly, P., Céilleachair, A., Skally, M., O'Leary, E., Staines, A., Kapur, K., Fitzpatrick, P. and Sharp, L., 2013. Time Costs Associated with Informal Care for Colorectal Cancer: An Investigation of the Impact of Alternative Valuation Methods. *Applied Health Economics and Health Policy*, 11(3), pp.193-203.

Jean-Claude, M., Emmanuelle, P., Juilette, H., Michele, B., Gerard, D., Eric, F., Xavier, H., Bertrand, L., Jean-Fabien, Z., Yves, P. and Gerard, N., 2012. Clinical and economic impact of malnutrition per se on the postoperative course of colorectal cancer patients. *Clinical Nutrition*, 31(1), pp.896-902.

Halligan, S., Dadswell, E., Wooldrage, K., Wardle, J., von Wagner, C., Lilford, R., Yao, G., Zhu, S. and Atkin, W., 2015. Computed tomographic colonography compared with

colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicentre randomised trials with economic evaluation (the SIGGAR trials). *Health Technology Assessment*, 19(54), pp.1-134.

Lansdorp-Vogelaar, I., Goede, S., Bosch, L., Melotte, V., Carvalho, B., van Engeland, M., Meijer, G., de Koning, H. and van Ballegooijen, M., 2018. Cost-effectiveness of High-performance Biomarker Tests vs Fecal Immunochemical Test for Noninvasive Colorectal Cancer Screening. *Clinical Gastroenterology and Hepatology*, 16(4), pp.504-512.

Laudicella, M., Walsh, B., Burns, E. and Smith, P., 2016. Cost of care for cancer patients in England: evidence from population-based patient-level data. *British Journal of Cancer*, 114(11), pp.1286-1292.

Lejeune, C., Binquet, C., Bonnetain, F., Mahboubi, A., Abrahamowicz, M., Moreau, T., Raikou, M., Bedenne, L., Quantin, C. and Bonithon-Kopp, C., 2009. Estimating the cost related to surveillance of colorectal cancer in a French population. *The European Journal of Health Economics*, 10(4), pp.409-419.

Lemmon, E., Hanna, C., Morris, E, and Hall, P., 2020. Health Economic Studies of Colorectal Cancer and the Contribution of Administrative Data: a Systematic Review. Pre-print DOI: https://doi.org/10.1101/2020.09.29.20203679

Macafee, D., West, J., Scholefield, J. and Whynes, D., 2009. Hospital Costs of Colorectal Cancer Care. *Clinical medicine. Oncology*, 3, pp.23-62.

Matter-Walstra, K., Schwenkglenks, M., Betticher, D., von Moos, R., Dietrich, D., Baertschi, D. and Koeberle, D., 2016. Bevacizumab Continuation Versus Treatment Holidays After First-Line Chemotherapy With Bevacizumab in Patients With Metastatic Colorectal Cancer: A Health Economic Analysis of a Randomized Phase 3 Trial (SAKK 41/06). *Clinical Colorectal Cancer*, 15(4), pp.314-320..

Michalpoulos, N., Theodoropoulos, G., Stamopoulos, P., Sergentanis, T., Memos, N., Tsamis, D., Flessas, I., Menenakos, E., Kontodimopoulos, N. and Zografos, G., 2013. A cost-utility analysis of laparoscopic vs open colectomy of colorectal cancer in a public hospital of the Greek National Health System. *J BUON*, 18(1), pp.86-97.

Murphy, J., Halloran, S. and Gray, A., 2017. Cost-effectiveness of the faecal immunochemical test at a range of positivity thresholds compared with the guaiac faecal occult blood test in the NHS Bowel Cancer Screening Programme in England. *BMJ Open*, 7(10), p.71-86.

Ó Céilleachair, A., Hanly, P., Skally, M., O'Neill, C., Fitzpatrick, P., Kapur, K., Staines, A. and Sharp, L., 2013. Cost Comparisons and Methodological Heterogeneity in Cost-of-illness Studies. *Medical Care*, 51(4), pp.339-350.

Pil, L., Fobelets, M., Putman, K., Trybou, J. and Annemans, L., 2016. Cost-effectiveness and budget impact analysis of a population-based screening program for colorectal cancer. *European Journal of Internal Medicine*, 32, pp.72-78.

Pilgrim, H., Tappenden, P., Chilcott, J., Bending, M., Trueman, P., Shorthouse, A. and Tappenden, J., 2009. The costs and benefits of bowel cancer service developments using discrete event simulation. *Journal of the Operational Research Society*, 60(10), pp.1305-1314.

Rao, C., Smith, F., Martin, A., Dhadda, A., Stewart, A., Gollins, S., Collins, B., Athanasiou, T. and Sun Myint, A., 2018. A Cost-Effectiveness Analysis of Contact X-ray Brachytherapy for the Treatment of Patients with Rectal Cancer Following a Partial Response to Chemoradiotherapy. *Clinical Oncology*, 30(3), pp.166-177.

Špacírová, Z., Epstein, D., García-Mochón, L., Rovira, J., Olry de Labry Lima, A. and Espín, J., 2020. A general framework for classifying costing methods for economic evaluation of health care. *The European Journal of Health Economics*, 21(4), pp.529-542.

Tan, S., 2009. *Microcosting In Economic Evaluations*. Erasmus Universiteit Rotterdam.

Tan, S., Rutten, F., van Ineveld, B., Redekop, W. and Hakkaart-van Roijen, L., 2009. Comparing methodologies for the cost estimation of hospital services. *The European Journal of Health Economics*, 10(1), pp.39-45.

WHO, 2020. *Colorectal Cancer*. [online] Euro.who.int. Available at: <https://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/news/news/2012/2/early-detection-of-common-cancers/colorectal-cancer> [Accessed 25 August 2020].

YHEC - York Health Economics Consortium. 2016. Discount Rate - YHEC - York Health Economics Consortium. [online] Available at: <https://yhec.co.uk/glossary/discount-rate/> [Accessed 16 October 2020].

6. Appendix

Table 1: Economic Evaluation Studies Summary								
General Information						Costing Specific Information		
Author (Year)	**Country of Study**	**Perspective (Specified)**	**Time Horizon**	**Part of Pathway**	**Study Type**	**Cost Sources**	**Discounting**	**Type of Costs**
Bullement et al. (2017)	UK	Healthcare Provider (Yes)	10-years	Treatment	CUA	Monthly Index of Medical Specialities; Lonsurf Price and Dosing Regimen; NICE Guidance	3.5% per annum	Direct
Halligan et al. (2014)	UK	Healthcare Provider (Yes)	5.2-years	Treatment	CEA	BNF; NHS Reference Costs	No	Direct
Kearns et al. (2014)	England	Healthcare Provider (Yes)	4-year	Screening	CUA	English Bowel Cancer Screening Program	3.5% per annum	Direct
Lansdorp-Vogelaar et al. (2018)	Netherlands	Societal (Yes)	Unspecified	Screening	CEA	Dutch Healthcare Authority Medical Cost Price Index; Dutch Erasmus Medical Centre; Netherlands Cancer Registry	3% per annum	Direct and Indirect
Matter-Walstra et al. (2016)	Switzerland	Healthcare Provider (Yes)	OS	Treatment	CEA	Unspecified	No	Direct
Michapoulos et al. (2013)	Greece	Healthcare Provider (Yes)	10-month	Treatment	CUA	Patient Questionnaires; European Association for Endoscopic Surgery	No	Direct
Murphy et al. (2017)	England	Healthcare Provider (Yes)	1-year	Screening	CUA	NHS Reference Costs; BCSP; Other CRC Literature	3.5% per annum	Direct
Pil et al. (2016)	Belgium	Societal (Yes)	20-year	Screening	CEA	Belgian Cancer Registry; Official Belgian Costs of Medical Procedures; Belgian Healthcare Knowledge Centre; Other CRC Literature	3% per annum	Direct and Indirect
Pilgrim et al. (2017)	England	Healthcare Provider (No)	Unspecified	Unspecified	CEA	Hospital Episode Statistics; NHS Reference Costs; NHS Cancer Screening Programmes; Other CRC Literature	3.5% per annum	Direct
Rao et al. (2018)	UK	Healthcare Provider (Yes)	Lifetime	Treatment	CUA	Hospital Episode Statistics; NHS Reference Costs; NICE	3.5% per annum	Direct

Table 2: Cost of Illness Studies Summary							
General Information					**Costing Specific Information**		
Author (Year)	**Country of Study**	**Perspective (Specified)**	**Time Horizon**	**Part of Pathway**	**Cost Sources**	**Discounting**	**Type of Costs**
Bending et al. (2010)	England	Healthcare Provider (No)	1-year	Entire Pathway	NHS Reference Costs; Hospital Episode Statistics; Unit Costs of Health and Social Care	No	Direct
Corral et al. (2016)	Spain	Healthcare Provider (Yes)	11-years	Treatment	Hospital Cancer Registry; Clinical Administrative System; Cost Accounting System	3% per annum	Direct
Francisci et al. (2013)	Italy	Unspecified (No)	1-year	Treatment	Population Based Cancer Registry; Hospital Discharge Cards; Reimbursement Costs	No	Direct
Guillani et al. (2013)	Italy	Healthcare Provider (No)	15-month	Treatment	Unspecified	No	Direct
Hall et al. (2014)	UK	Healthcare Provider (No)	15-month	Treatment	Patient Finance Data	No	Direct
Hanly et al. (2013)	Ireland	Societal (Yes)		Treatment	Cancer Registry Ireland; National Gross Mean Earnings; National Minimum Wage	No	Indirect
Jean-Claude et al. (2012)	France	Healthcare Provider (No)	4-month	Treatment	French National Cost Construction Study; Reimbursement Costs	No	Direct
Laudicella et al. (2016)	England	Healthcare Provider (No)	9-year	Treatment	National Cancer Data Repository; Hospital Episode Statistics; National Schedule of Reference Costs	No	Direct
Lejeune et al. (2009)	France	Health Insurance (No)	3-year	Surveillance	Reimbursement Costs; Nomenclature Generale des Actes Professionels; Nomenclature des Actes de Biologie Medicale; Classification Communie des Actes Medicaux	No	Direct
Macaffe et al. (2009)	England	Healthcare Provider (No)	21-year	Treatment	NHS Reference Costs; Hospital Finance Department; Nottingham City Hospital Pharmacy	3% per annum	Direct