Original Study

Three Versus Six Months of Adjuvant Doublet Chemotherapy for Patients With Colorectal Cancer: A Multi-Country Cost-Effectiveness and Budget Impact Analysis

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Abstract

This study widens the transferability of cost–utility results from the SCOT trial showing that administering 3 months of adjuvant, oxaliplatin-based chemotherapy is cost-effective and cost saving compared to 6 months from the perspective of all countries recruited to SCOT. The impact on healthcare budgets if the findings are implemented as predicted will amount to savings of at least US$150 million over 5 years.

Background: The Short Course Oncology Treatment (SCOT) trial demonstrated non-inferiority, less toxicity, and cost-effectiveness from a UK perspective of 3 versus 6 months of oxaliplatin-based chemotherapy for patients with colorectal cancer. This study assessed the cost-effectiveness of shorter treatment and the budget impact of implementing trial findings from the perspectives of all countries recruited to SCOT: Australia, Denmark, New Zealand, Spain, Sweden, and the United Kingdom. **Patients and Methods:** Individual cost–utility analyses were performed from the perspective of each country. Resource, quality of life, and survival estimates from the SCOT trial ($N = 6065$) were used. Probabilistic sensitivity analysis and subgroup analyses were undertaken. Using undiscounted costs from these cost–utility analyses, the impact on country-specific healthcare budgets of implementing the SCOT trial findings was calculated over a 5-year period. The currency used was US dollars (US$), and 2019 was the base year. One-way and scenario sensitivity analysis addressed uncertainty within the budget impact analysis. **Results:** Three months of treatment were cost saving and cost-effective compared to 6 months from the perspective of all countries. The incremental net monetary benefit per patient ranged from US$8972 (Spain) to US$13,884 (Denmark). The healthcare budget impact over 5 years for the base-case scenario ranged from US$3.6 million (New Zealand) to US$61.4 million (UK) and totaled over US$150 million across all countries. **Conclusion:** This study has widened the transferability of results from the SCOT trial, showing that shorter treatment is cost-effective from a multi-country perspective. The vast savings from implementation could fully justify the investment in conducting the SCOT trial.

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Introduction

Adjuvant chemotherapy offers a survival benefit for patients with colorectal cancer (CRC), but at the expense of toxicity.[1-5] When oxaliplatin-based treatment is used, peripheral nerve damage is a particular concern.[6] The Short Course Oncology Treatment (SCOT) trial[7] demonstrated that 3 months of adjuvant, fluoropyrimidine–oxaliplatin chemotherapy was noninferior compared with 6 months of treatment and demonstrated significantly less toxicity. In particular, the percentage of patients experiencing ≥grade 2 peripheral neuropathy was less than half in the 3-month arm versus the 6-month arm.[7]

Clinical effectiveness of CRC treatments is the key consideration for clinicians and policymakers. However, due to the high disease burden and substantial cost of treating CRC,[8] assessing the cost-effectiveness of novel treatments is important and often a requirement of health technology assessment authorities globally.[9] In addition, even if a new treatment is cost-effective, this does not illustrate the economic implications of using the new treatment approach in practice. Several health technology assessment authorities now also require a budget impact analysis (BIA) to estimate the monetary impact of implementing a new strategy and displacing the current standard of care within their healthcare service.[10]

Multinational trials, such as SCOT, have several advantages. Patient recruitment is expedited, patients from several countries are given the opportunity to participate in research, and the generalizability of clinical results is widened.[11,12] The transferability of cost-effectiveness estimates among countries, however, is not straightforward. This is partly due to heterogeneity in unit costs, the varying structures of healthcare systems, and the various thresholds used by decision makers to assess whether a treatment is considered good value for money.[12-15] Nonetheless, if health economic data within a trial have been collected from different locations, it is important that attempts are made to provide value estimates for all participating countries.[12,16] Three months of adjuvant, doublet chemotherapy for CRC has previously been shown to be cost-effective compared with 6 months from the perspective of the UK National Health and Personal Social Services.[17]

The aim of this study was to estimate the value, and economic implications of using a shorter duration of adjuvant treatment for patients with CRC across all locations that recruited patients to SCOT. The main objectives were to (1) evaluate the cost-effectiveness of 3 versus 6 months of adjuvant, oxaliplatin-based chemotherapy for patients with CRC from the perspective of the healthcare systems in Australia, Denmark, New Zealand, Spain, Sweden, and the UK; and (2) estimate the budget impact in these countries if the SCOT trial findings were implemented.

Methods

First, demographic, disease, and treatment-related characteristics for patients enrolled in SCOT from each country were assessed. Non-adjusted, average (median) compliance with fluoropyrimidine and oxaliplatin therapy was calculated specific to patients from each country.

An analysis of the cost-effectiveness of using shorter treatment from the perspective of each individual country was performed, followed by an evaluation of the likely budget implications of introducing shorter treatment in each location. The approach used for each assessment is described in detail in Supplemental Table 1A (per CHEERS reporting guideline[18]; see the online version at doi:10.1016/j.clcc.2021.04.001) and Supplemental Table 3A (per BIA ISPOR guideline[10]; see the online version at doi:10.1016/j.clcc.2021.04.001).

For both analyses, a healthcare system perspective was adopted, and calculations were performed in US dollars (US$) unless otherwise specified, with 2019 as the base year. Health-specific purchasing power parity[19] was used to convert country-specific costs to US dollars. The sources of chemotherapy medication costs are shown in Table 2A (see the online version at doi:10.1016/j.clcc.2021.04.001). For hospitalization unit costs, results from the World Health Organization Choice project[20] were utilized to calculate the ratio of between-country differences in inpatient and outpatient costs, using the United Kingdom as the reference country. This ratio was applied to the Scottish Information Services Division 2019 unit costs relevant to hospitalization resource use collected within the SCOT trial.

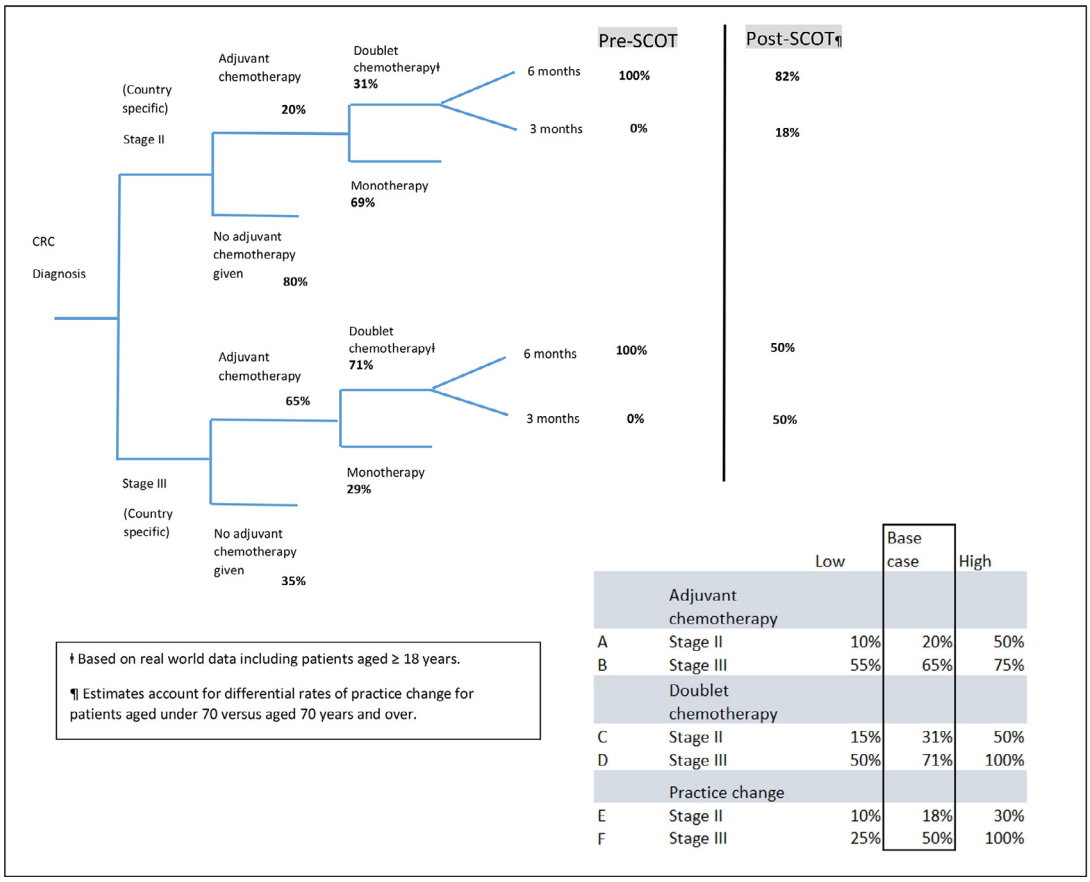
Analysis of Cost-Effectiveness

A 10-year within-trial time horizon was used, with extended follow-up compared to the previous cost–utility analysis (CUA).[17] Quality adjusted life-years (QALYs) were estimated using partitioned survival analysis with Kaplan–Meier estimates of time on treatment, disease-free survival after treatment, and recurrence, weighted by health utilities, which were calculated by applying country-specific preferences.[21,22-26] EQ-5D responses were available for a subgroup of patients ($n = 1832$); therefore, linear regression analysis was used to adjust for health state (time on treatment, disease-free survival, and recurrence), regimen received, disease risk, age, gender, and ethnicity. For years 0 to 6, average costs for patients in both arms of the trial, accrued over prespecified time intervals, were adjusted for the probability that a patient in that arm of the trial survived to the start of the time point using the Kaplan–Meier estimator. For year 7, resource use data presented a considerable level of missing information, and no data were available for years 8 to 10. Therefore, a model estimated yearly costs after controlling for trial arm, time from randomization, and the same covariates included in the utility model.

To estimate the cost-effectiveness of shorter treatment for each country, six fully pooled, single-country costing analyses were undertaken.[27,28] Outcomes and resource use from all countries were pooled, and country-specific unit costs and utility scores were applied to resource use and EQ-5D answers, respectively, for all patients in the trial. No adjustment was made for clustering at the country level within the survival analysis. A fully pooled, multi-country costing analysis was also performed and used for subgroup analyses. The multi-country approach pooled outcome and resource use data but applied unit costs and utilities specific to the location from which each individual patient was recruited.

The incremental net monetary benefit (INMB) of using 3 months versus 6 months was calculated using a willingness to pay (WTP)/QALY threshold of one gross domestic product per capita for each country.[29] Both costs and outcomes after year 1 were discounted at a rate of 3.5% per annum. Probabilistic sensitiv-

Figure 1 Summary of Estimation of Eligible Population for Budget Impact Analysis and Parameters Used in a Sensitivity Analysis. Abbreviations: CRC = colorectal cancer; SCOT = Short Course Oncology Treatment.



		Low	Base case	High
	Adjuvant chemotherapy			
A	Stage II	10%	20%	50%
B	Stage III	55%	65%	75%
	Doublet chemotherapy			
C	Stage II	15%	31%	50%
D	Stage III	50%	71%	100%
	Practice change			
E	Stage II	10%	18%	30%
F	Stage III	25%	50%	100%

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ity analysis was undertaken to account for uncertainty regarding costs, QALYs, and cost-effectiveness outcomes using bootstrapping with 1000 iterations; the results are presented as confidence intervals around point estimates.[17] Deterministic sensitivity analysis was undertaken to explore the INMB for 3 months versus 6 months of treatment over a range of WTP thresholds.

Analysis of Budget Impact

Figure 1 outlines the approach used for the BIA. The eligible population consisted of patients diagnosed with stage II or III CRC who receive adjuvant oxaliplatin-based doublet chemotherapy. The number of patients diagnosed with CRC in each country was derived from the published literature, and an estimate of the proportion of patients who receive adjuvant chemotherapy, and those who receive doublet treatment specifically, was applied (see Supplemental Table 4A in the online version at doi:10.1016/j.clcc.2021.04.001).

Rather than assuming that all patients would receive shorter treatment after the SCOT trial findings were disseminated, an international clinician survey (April 2019) was used to estimate practice change (see Supplemental Table 4A in the online version at doi:10.1016/j.clcc.2021.04.001).[30] The survey estimates accounted for differences in practice changes for patients under 70 years of age versus 70 years and over. A cost calculator in Microsoft Excel 2016 was used to calculate the country-specific budget impact for a base-case scenario over 5 years. Average undiscounted per-patient costs for chemotherapy medication and hospitalization resource utilization per annum for years 1 to 5 from each arm of the SCOT trial specific to each country were used. Uncertainty regarding key parameters (Figure 1) in the BIA was addressed in a one-way sensitivity analysis. In addition, a scenario analysis was performed to exclude patients with rectal cancer and to look at the budget impact relevant to patients with stage II CRC and stage II/III colon cancer separately.

Results

Country-specific characteristics for SCOT trial patients (N = 6055) are shown in Table 1. Notable differences included the fact that Australian clinicians preferred leucovorin calcium (folinic acid), fluorouracil, and oxaliplatin (FOLFOX; 78%), whereas those from Denmark, New Zealand, and the United Kingdom preferred capecitabine and oxaliplatin (CAPOX). There was a relatively even split of CAPOX versus FOLFOX use for patients from Sweden and

Table 1 Differences in Patient, Disease, and Treatment Characteristics Among Patients Recruited From Different Countries in the SCOT Trial (N = 6065)

	Australia (*n* = 196, 3.2)	Denmark (*n* = 310, 5.1)	New Zealand (*n* = 16, 0.3)	Spain (*n* = 233, 3.8)	Sweden (*n* = 82, 1.4)	United Kingdom (*n* = 5228, 86.2)
Patient Characteristics						
Age (y)						
Mean (min/max)	64 (39/83)	64 (23/81)	65 (48/78)	63 (38/80)	63 (32/78)	63 (20/85)
Median (IQR)	65 (58-71)	65 (59-70)	66 (61-71)	64 (57-69)	65 (59-69)	65 (58-70)
Gender, *n* (%)						
Male	112 (57)	178 (57)	11 (69)	143 (61)	51 (62)	3177 (61)
Female	84 (43)	132 (43)	5 (31)	90 (39)	31 (38)	2051 (39)
Performance status, *n* (%)						
0	160 (82)	248 (80)	12 (75)	180 (77)	75 (91)	3642 (70)
1	36 (18)	62 (20)	4 (25)	53 (23)	7 (9)	1586 (30)
Disease Characteristics						
Extended risk stage, *n* (%)						
II	4 (2)	85 (27)	0 (0)	62 (27)	7 (9)	956 (18)
Low III	117 (60)	129 (42)	8 (50)	99 (42)	34 (41)	2281 (44)
High III	75 (38)	96 (31)	8 (50)	72 (31)	41 (50)	1991 (38)
Treatment						
Drug regimen, *n* (%)						
FOLFOX	152 (78)	45 (15)	4 (25)	110 (47)	40 (49)	1620 (31)
CAPOX	44 (22)	265 (85)	12 (75)	123 (53)	42 (51)	3608 (69)
Treatment Compliance (%), Median (IQR)						
Fluoropyrimidine						
3 mo	97 (89-99)	94 (86-98)	91 (87-96)	97 (91-99)	93 (88-98)	94 (81-99)
6 mo	90 (58-97)	79 (49-92)	79 (65-92)	92 (80-98)	85 (59-96)	82 (56-94)
Oxaliplatin						
3 mo	97 (89-99)	87 (63-97)	99 (90-100)	98 (93-99)	95 (87-98)	95 (81-99)
6 mo	70 (53-87)	43 (25-66)	78 (74-79)	85 (60-97)	62 (37-72)	70 (45-86)

Abbreviations: CAPOX = capecitabine and oxaliplatin; FOLFOX = leucovorin calcium (folinic acid), fluorouracil, and oxaliplatin; IQR = interquartile range.

Spain. No patients with stage II disease were recruited from New Zealand, although the overall number from this country was small. Unsurprisingly, treatment compliance was better for the 3-month trial arm, and compliance with fluoropyrimidine exceeded that for oxaliplatin across both arms and all countries.

Costs

The average undiscounted chemotherapy and hospitalization cost per patient for each country of using 3 months versus 6 months of treatment and differences in treatment durations are shown in Figure 2. Costs calculated using a multi-country approach aligned closely with those from the United Kingdom because most patients in the SCOT trial were from this location.

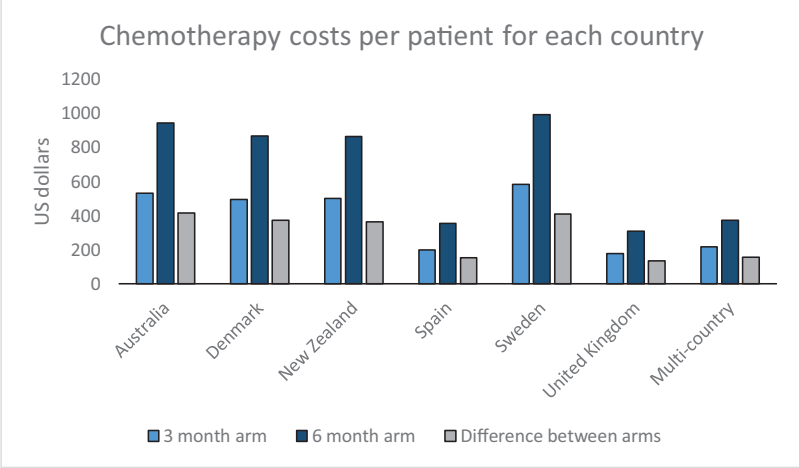
Outcomes

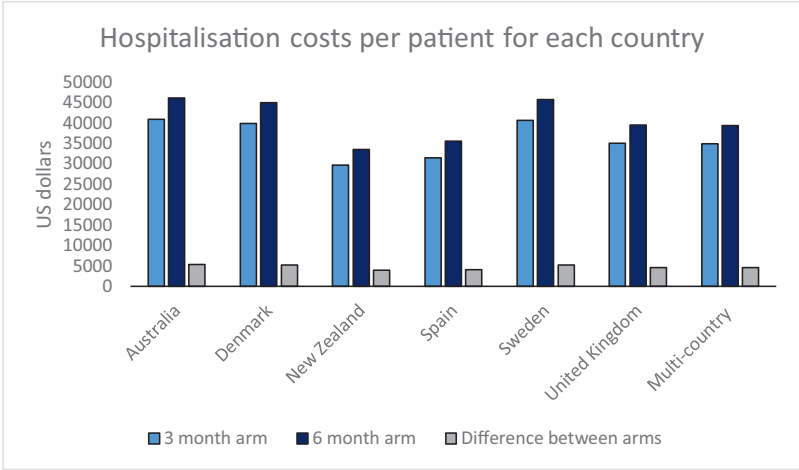
Supplemental Figure 2B (see the in the online version at doi:10.1016/j.clcc.2021.04.001) shows the Kaplan–Meier survival curves used for the purposes of this analysis. Using 10-year survival data, restricted mean life expectancy (see Supplemental Table A6 in the online version at doi:10.1016/j.clcc.2021.04.001; not statistically significant) was higher for patients in the 3-month versus 6-month arm. Supplemental Figure 3B (see the in the online version at doi:10.1016/j.clcc.2021.04.001) demonstrates the change in quality-of-life estimates over time calculated using country-specific utility weights. Overall, health-related quality-of-life estimates were lowest for New Zealand and highest for Sweden. QALY gains for the 3-month versus 6-month treatment strategy ranged from 0.11 for Sweden to 0.17 for New Zealand (Table 2).

Cost Utility, Sensitivity, and Subgroup Analyses

Overall, 3 months of treatment was a dominant strategy compared with 6 months across all locations. The INMB was greater than US$8000, with over 99% probability that the 3-month arm was cost-effective for all countries at a WTP threshold of one gross domestic product per capita. Figure 3 demonstrates the INMB across a range of WTP thresholds. Sweden had one of the highest cost savings; therefore, at lower WTP it provided the highest INMB. As the WTP for a QALY gain increased, the INMB was highest from a New Zealand perspective because of the highest QALY gain when New Zealand-specific EQ-5D weights were applied to the calculation of utilities. The cost-effectiveness acceptability curve and cost-effectiveness plane for each location

Figure 2 Mean Undiscounted Costs Per Patient Per Arm and Differences Between Trial Arms for Each Country Using a Fully Pooled Costing Approach and a Multi-Country Perspective Using a Multi-Country Costing Approach for a, chemotherapy medication costs and b, hospitalization costs.





are shown in Supplemental Figure 4B (see the online version at doi:10.1016/j.clcc.2021.04.001). Subgroup analysis results are provided in Supplemental Figure 5B (see the online version at doi:10.1016/j.clcc.2021.04.001). There was most uncertainty in cost-utility estimates for patients receiving FOLFOX. At a WTP threshold of US$42,000, the probability of 3 months of FOLFOX being cost-effective was 77% compared with 99% for CAPOX.

Analysis of Budget Impact

The healthcare system savings of implementation of SCOT trial findings over 5 years ranged from US$3.6 million (New Zealand) to over US$61.4 million (United Kingdom) (Table 3; Table for country-specific currency, see also Supplemental Table A7 in the online version at doi:10.1016/j.clcc.2021.04.001). The combined base-case budget impact was US$152 million. The impact for New Zealand was lowest due to the smallest eligible population and cost difference per patient. Although the eligible population in Spain was higher than in the United Kingdom, higher per-patient cost savings from a UK perspective led to larger estimated budget savings.

BIA Sensitivity Analysis

In a one-way sensitivity analysis (see Supplemental Figure 6B in the online version at doi:10.1016/j.clcc.2021.04.001), when it was assumed that all patients with stage III CRC received 3 months rather than 6 months of adjuvant doublet chemotherapy following dissemination of SCOT trial findings, the overall potential budget savings amounted to US$297 million. Removing patients with stage II disease from the analysis (Table 3; see Supplemental Figure 6B in the online version at doi:10.1016/j.clcc.2021.04.001) had little effect (total budget impact, US$145 million) because of the small stage II CRC population deemed eligible to be affected by a practice change in the base scenario. Excluding patients with rectal cancer in a scenario analysis led to a decrease in the budget impact by less than half (total impact of US$102 million).

Table 2 Country-Specific Cost–Utility Analysis Results

Arm	Mean (Discounted) Costs, US$ (95% CI)	QALYs (95% CI)	NMB Using a WTP Threshold of One GDP (Country-Specific) per Capita, US$ (95% CI)	Probability of Being CE at WTP of 1× GDP per Capita (%)
Australia			GDP for Australia: 53,000	
3 mo	37,289 (35,520-39,226)	6.28 (6.17-6.40)	295,494 (288,886-302,170)	99.6
6 mo	42,830 (40,691-44,999)	6.13 (6.00-6.26)	282,158 (275,037-239,783)	0.4
Incremental	–5541 (–8383 to 2624)	0.14 (–0.01 to 0.30)	13,337 (4265-22,533)	3M dominates
Denmark			GDP for Denmark: 62,000	
3 mo	36,357 (34,639-38,242)	6.35 (6.25-6.47)	357,653 (350,583-365,053)	99.6
6 mo	41,744 (39,660-43,856)	6.22 (6.10-6.34)	343,768 (335,926-352,194)	0.4
Incremental	–5386 (–8156 to 2544)	0.13 (–0.01 to 0.28)	13,884 (4011-24,119)	3M dominates
New Zealand			GDP for New Zealand: 42,000	
3 mo	27,133 (25,889-28,514)	5.80 (5.67-5.93)	216,261 (210,639-222,158)	99.6
6 mo	31,264 (29,736-32,793)	5.63 (5.49-5.77)	204,983 (198,714-211,365)	0.4
Incremental	–4131 (–6148 to 2013)	0.17 (0.002-0.34)	11,278 (3886-19,311)	3M dominates
Spain			GDP for Spain: 31,000	
3 mo	28,443 (27,119-29,909)	6.44 (6.33-6.56)	171,245 (167,196-175,464)	99.8
6 mo	32,583 (30,961-34,217)	6.29 (6.16-6.41)	162,273 (158,018-166,987)	0.2
Incremental	–4,140 (–6286 to 1893)	0.15 (–0.00 to 0.31)	8972 (3409-14,602)	3M dominates
Sweden			GDP for Sweden: 52,000	
3 mo	37,104 (35,244-39,079)	6.56 (6.46-6.65)	303,778 (298,231-309,245)	99.5
6 mo	42,515 (40,353-44,770)	6.44 (6.34-6.54)	292,493 (286,508-298,774)	0.5
Incremental	–5411 (–8383 to 2418)	0.11 (–0.02 to 0.24)	11,285 (3557-18,942)	3M dominates
United Kingdom			GDP for United Kingdom: 40,000	
3 mo	31,629 (30,144-33, 269)	6.27 (6.16-6.39)	219,347 (214,184-224,628)	99.6
6 mo	36,182 (34,368-38,023)	6.12 (5.99-6.25)	208,673 (203,051-214,704)	0.4
Incremental	–4553 (–6955 to 2056)	0.15 (–0.01 to 0.31)	10,674 (3683-17,928)	3M dominates
Multi-country			NICE threshold: £30,000 (US$42,000)	
3 mo	31,594 (30,092-33,227)	6.27 (6.16-6.39)	231,932 (226,577-237,410)	99.6
6 mo	36,150 (34,333-38,008)	6.12 (6.00-6.25)	220,949 (215,104-227,210)	0.4
Incremental	–4557 (–6932 to 2097)	0.15 (–0.01 to 0.31)	10,983 (3684-18,664)	3M dominates

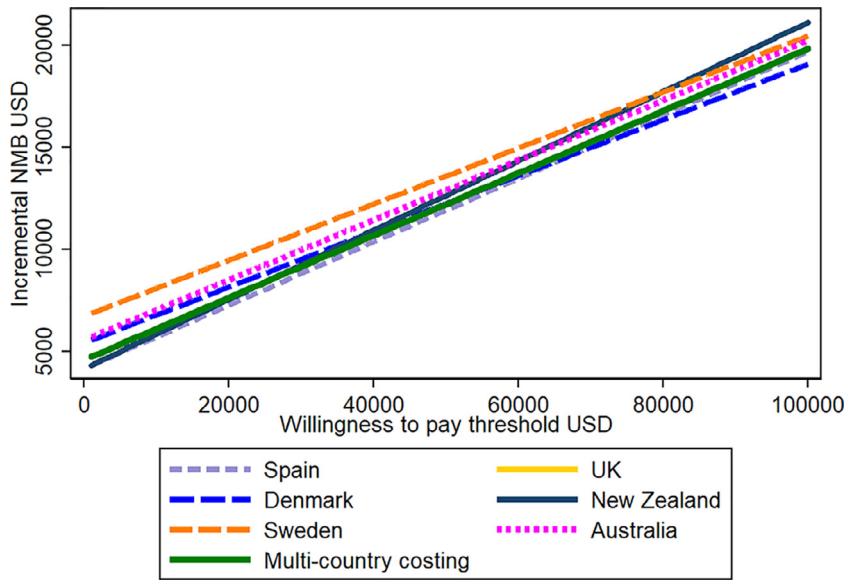
Abbreviations: 3M = 3 months; CE = cost-effective; CI = confidence interval; GDP = gross domestic product; NICE = National Institute for Health and Clinical Excellence; NMB = net monetary benefit; QALYs = quality adjusted life-years; WTP = willingness to pay.

Table 3 BIA Base Case and Scenario Analysis in Country-Specific Currency

	US$					
	Australia	Denmark	New Zealand	Spain	Sweden	United Kingdom
Base Scenario Budget Impact						
Chemotherapy medication costs over 5 y	2.0	0.5	0.3	1.8	0.8	1.9
Treatment-related hospitalizations in (year 1 for each individual patient) over 5 y	21.4	6.5	3.1	40.2	8.8	56.1
Condition-related hospitalizations (years 2-5 for each individual patient) over 5 y	1.3	0.4	0.2	2.4	0.6	3.4
Total budget impact = medication cost + cost of treatment and condition-related hospitalizations	24.7	7.4	3.6	44.4	10.2	61.4
Scenario Analysis (Per Base Scenario)						
Colon cancer only	17.1	5.0	2.4	29.2	6.9	41.3
Stage III only (CRC)	23.5	7.1	3.4	42.4	9.8	58.7
Stage III only (colon cancer)	16.3	4.7	2.3	27.9	6.6	39.5
Stage II only (colon cancer)	0.8	0.2	0.1	1.3	0.3	1.8

All values for budget impact included in this table indicate cost savings.
Abbreviation: CRC = colorectal cancer.

Figure 3 Incremental NMB Over a Range of WTP Thresholds for Each Country (Fully Pooled, One-Country Costing Analysis) and Using a Fully Pooled, Multi-Country Costing Analysis. UK and Multi-Country Results Are Overlapping. Abbreviations: NMB = net monetary benefit; USD = US dollars; WTP = willingness to pay.



Discussion

Adjuvant, oxaliplatin-based chemotherapy for 3 months is cost-effective and cost saving compared to 6 months from the perspective of all countries that recruited patients to the SCOT trial. Using survival data with follow-up until 10 years, mean life expectancy was better in the 3-month arm (not statistically significant), whereas in the previous CUA (8-year follow-up) life expectancy was non-significantly higher in the 6-month arm.[17] Also, although there was a QALY gain from shorter treatment in the previous CUA, it was higher in this study (only statistically significant for New Zealand), driven both by increased life expectancy and quality-of-life improvement. These results have updated the cost-effectiveness analysis from a UK perspective by using the most recently available survival data and have increased the relevance of the CUA to clinicians from other countries. Specifically, clinicians and policymakers will now have country-specific estimates of QALY gains and cost savings to guide their decision making.

Subgroup analysis revealed that the cost-effectiveness of using 3 months versus 6 months of treatment was less certain for patients receiving FOLFOX, especially at higher WTP thresholds. This was because of the small mean benefit in life expectancy from using longer treatment with this regimen (not statistically significant). There may be patient- or disease-specific factors that affect clinician preference for using FOLFOX rather than CAPOX for an individual patient, such as the presence of an ileostomy, difficulty swallowing tablets, or concerns regarding compliance with oral medication. In combination with updated clinical effectiveness results from SCOT and the other International Duration Evaluation of Adjuvant Chemotherapy (IDEA) collaboration trials,[31,32] clinicians can use the information from this study when making decisions on treatment duration for patients in whom FOLFOX is their regimen of choice. This study has also provided cost-effectiveness estimates for low- and high-risk stage III disease and stage II disease with high-risk features. Such estimates provide additional information compared with the previous CUA, which split risk stage using a binary division between patients with high-risk stage III disease versus low-risk stage III and stage II disease combined.

Approximately 1.8 million people[33] are diagnosed with CRC per annum globally, with the cost of managing this disease projected to be over US$39 billion[34]; around half of these patients[35] present with stage II or III disease. Making savings relevant to this patient cohort therefore has significant cost consequences for healthcare systems globally. This study shows that implementing SCOT trial findings in six high-income countries translates to savings of hundreds of millions of dollars, and the total global impact is likely to be several times this estimation. This study used a relatively conservative estimate of practice change, based on a large clinician survey conducted in April 2019 and adjusted for the likely proportion of patients actually receiving adjuvant chemotherapy after surgical resection and a reduced use of doublet chemotherapy versus monotherapy in older patients. The findings from the BIA sensitivity analysis using a higher level of practice change may be useful to country-specific decision makers if they know that the proportion of patients receiving 3 months of doublet chemotherapy in their location is higher than the average estimate used in this study.

In addition to providing useful information to country-specific decision makers, this study also provides an estimate of the longer term consequences of conducting the SCOT trial. Specifically,

the results demonstrate how the magnitude of healthcare system savings compare to the project-specific funding invested by charities and research councils to conduct the SCOT trial (see the funding section of Supplemental Table 3A in the online version at doi:10.1016/j.clcc.2021.04.001). Although the charities and research councils that invested in SCOT will not recoup these costs directly, many cancer research funders are interested in knowing that their investments are leading to societal impact, which includes economic benefits for healthcare systems.[36-39]

This study has some important limitations. First, when using a fully pooled approach, varying unit costs alone is likely to underestimate between-country differences compared with fully splitting the analyses.[12] For the purposes of the BIA, an assumption was made that the clinicians who reported that they prescribed 3 months of doublet chemotherapy after SCOT used 6 months of doublet chemotherapy before SCOT. There is most uncertainty surrounding how this applies to patients with stage II disease, because improvement in overall survival from adding oxaliplatin to fluoropyrimidine has not been demonstrated for this patient group[40,41]; for this reason, clinicians may give fluoropyrimidine monotherapy in this situation. This uncertainty was addressed by excluding patients with stage II disease within the BIA scenario analysis.

Also, despite being included in several international guidelines, the use of doublet chemotherapy in the adjuvant setting for rectal cancer is more controversial compared with its use for colon cancer, with fewer randomized trials to support its use. The budget change estimates for rectal cancer were therefore more uncertain compared with those for colon cancer and the reason why patients with rectal cancer were excluded within a sensitivity analysis. Finally, the BIA assumed that the proportion of patients receiving FOLFOX versus CAPOX before and after SCOT was the same as in the SCOT trial.[7] Given the higher uncertainty regarding the non-inferiority of using 3 months of FOLFOX, clinicians may switch to CAPOX. This is most relevant to clinicians from Australia, who showed a preference for FOLFOX within the SCOT trial.

Conclusion

This study has widened the transferability of cost–utility results from the SCOT trial. We encourage this type of analysis alongside multinational clinical trials to ensure that all countries that recruited patients to the trial have results relevant to their decision makers. This study has also estimated a 5-year healthcare budget impact of implementing SCOT trial findings of over US$150 million across six countries over 5 years. These savings could fully justify the investment in conducting the SCOT trial.

Clinical Practice Points

- What is already known? Administering 3 months of adjuvant oxaliplatin-base chemotherapy is cost-effective compared with 6 months from a UK perspective. Prior to this study, it was not clear if these results were transferrable to patients from other countries or what the real-world cost savings of implementing shorter treatment would be.
- What are the new findings? Using updated survival data from the SCOT trial, this study has demonstrated that shorter treatment is still cost-effective compared with 6 months of chemotherapy from a UK perspective. Additional analyses have provided cost-effectiveness estimates from the perspectives of the five other countries that were also recruited to SCOT and have shown that 3 months of chemotherapy can be both cost-effective and offer cost savings across all locations and over a range of willingness-to-pay thresholds. In this study, the cost savings of implementing SCOT trial findings have been estimated using country-specific medication and hospitalization unit costs and total at least US$150 million over 5 years.
- How might these findings impact clinical practice in the foreseeable future? UK and international clinicians and policymakers will now have contemporary and country-specific cost-effectiveness estimates to supplement clinical efficacy results from SCOT when making decisions. The budget impact results will be particularly useful to clinicians involved in healthcare resource allocation and those who are interested in understanding the wider impacts from implementation of clinical trial findings. Specifically, the budget impact results can be used by clinician trialists to advocate for funding investment in future cancer trials.

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Disclosure

The authors have stated that they have no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clcc.2021.04.001.

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