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# BMJ Open

## Economic evaluation of different routes of surgery for the management of endometrial cancer: A retrospective cohort study.

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3 **1 Economic evaluation of different routes of surgery for the management of endometrial**  
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5 **2 cancer: A retrospective cohort study.**  
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20 **Word count: 3202**  
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3 **23 ABSTRACT**  
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6 **24 Objectives:** The benefits of minimally invasive surgery (MIS) for endometrial carcinoma (EC)  
7  
8 are well established although the financial impact of robotic-assisted hysterectomy (RH)  
9  
10 compared to laparoscopic hysterectomy (LH) is disputed.  
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13  
14 **27 Design:** Retrospective cohort study.  
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17 **28 Setting:** English NHS hospitals 2011-2017/8.  
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19  
20 **29 Population:** 35,304 women having a hysterectomy for EC identified from Hospital Episode  
21  
22 Statistics (HES).  
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24

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26 **31 Methods:** Analysis of Hospital Episode Statistics (HES) for England 2011-2017/18 for all  
27  
28 women undergoing an open (OH) or MIS (LH/RH) for EC. Costing data was analysed by each  
29  
30 surgical approach by age, Charlson Comorbidity Index (CCI) and hospital MIS rate  
31  
32 classification. The average marginal effect (AME) was calculated to compare RH vs OH/RH  
33  
34 vs LH which adjusted for any differences in the characteristics of the surgical approaches.  
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38 **36 Main outcome measures:** The association between route of surgery on cost at intervention,  
39  
40 30, 90 and 365 days.  
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43 **38 Results:** A total of 35,304 procedures were performed, 20,405 (57.8%) were MIS (LH 18,604  
44  
45 and RH 1,801), 14,291 (40.5%) OH. Mean cost for LH was significantly less than RH, whereas  
46  
47 RH was significantly less than OH at intervention, 30, 90 and 365 days ( $p < 0.001$ ). Overtime  
48  
49 patients who underwent RH became increasingly complex and by the 2015/16 year had a higher  
50  
51 average CCI than LH. Comparing the cost of LH and RH against CCI score identified that the  
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53 costs closely reflected the patients' CCI. There was also increasing disparity between the MIS  
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55 and OH costs with rising age. When exploring the association between provider volume, MIS  
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3 45 rate and surgical costs there was an association with the higher the MIS rate the lower the  
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6 46 average cost.  
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9 47 **Conclusions:** The cost of surgery was influenced by the level of patients' co-morbidities rather  
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11 48 than the route of surgery alone. Further research is needed to investigate costs in matched  
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13 49 populations to determine optimum surgical modality in different populations.  
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22 52 **Funding:** HCD economics were funded by Intuitive Surgical, Award/Grant number is not  
23  
24 53 applicable. None of the clinicians involved in this study received funding from Intuitive  
25  
26 54 Surgical. Intuitive Surgical did not have any involvement with the study design, data analysis  
27  
28  
29 55 and writing of the manuscript.  
30

31  
32 56 **Key words:** Endometrial cancer; minimally invasive surgery; laparoscopic hysterectomy; open  
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34 57 hysterectomy; robotic-assisted hysterectomy; cost  
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40 59 **Tweetable abstract:** Analysis of financial cost of laparoscopic, robotic and open hysterectomy  
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42 60 for the treatment of endometrial cancer in England.  
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3 67 ***Strengths and limitations***  
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- 6 68 • The findings from the study are based on a population-based database which is a key  
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8 69 strength as it is representative of all procedures via the NHS in England.  
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10  
11 70 • The reliability of the coding might have changed over time although there was no  
12  
13 71 evidence of changes in treatment coding or significant changes in the underlying study  
14  
15 72 population.  
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17  
18 73 • HES database reliably captures extensive amount of demographic, diagnosis and  
19  
20 74 procedure outcomes however there is a lack of cancer stage information therefore it is  
21  
22 75 not possible to split out the cost outcomes into more specific groups of patients.  
23  
24  
25 76 • The capital and maintenance costs of RH have also not been included since these costs  
26  
27 77 vary dramatically across different healthcare settings and often utilised by a wide group  
28  
29 78 of specialities in a hospital setting.  
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31  
32 79 • As the analysis was undertaken over a number of years of the HES database, we were  
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34 80 able to accurately follow hospital activity for at least a year after intervention.  
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## 89 INTRODUCTION

90 The introduction of minimally invasive surgery (MIS) for endometrial cancer (EC) has had a  
91 dramatic impact on patients' surgical outcomes with reduced morbidity, hospital stay and  
92 improved short-term quality of life<sup>1</sup>. Translating these patient benefits into cost benefits to the  
93 healthcare economy has been challenging because although MIS requires significantly less bed  
94 days than open surgery, it does require more costly consumable equipment, for example single-  
95 use vessel sealing devices. This has been demonstrated in several studies including the multi-  
96 centre randomised LACE trial where the surgery costs were greater for laparoscopic  
97 hysterectomy (LH) compared to open hysterectomy (OH), but the overall costs of treatment  
98 were lower<sup>2</sup>.

99 MIS is the preferred surgical route for EC<sup>3</sup>. RH is accepted as an alternative to LH, supported  
100 by evidence from a randomised controlled trial<sup>4</sup> and RH has been shown to have a lower  
101 conversion rate to laparotomy and shorter operating time<sup>5-7</sup>. Wide spread adoption of RH is  
102 limited in England, although the number of EC cases having RH increasing year on year<sup>8</sup>. In  
103 light of the capital and consumable costs of RH, as compared to OH or LH, the use of RH in  
104 EC is therefore being called into question<sup>6</sup>. Reports from institutions with well-established  
105 robotic programmes however have contested this view with no significant difference<sup>9</sup>, or cost  
106 improvements reported as compared to LH<sup>10</sup>. What is clear is that focusing solely on in-hospital  
107 costs does not give the full picture of the economic costs of a surgical procedure, since many  
108 costs are accrued following discharge or attributed to the economy as a whole as a result of  
109 delayed return to employment.

110 We therefore investigated the HES data for England in order to look at the financial impact of  
111 RH as compared to LH and OH. We also investigated the patient characteristics that contributed



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3 112 to cost and examined the top 5% of procedures to identify factors that may have contributed to  
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5 113 the costs.

## 114 **METHODS**

### 115 *Data Source and cohort selection*

116 Data was sourced from the Hospital Episode Statistics (HES) database from 2011-2017/8<sup>11</sup>.  
117 HES database captures demographic, diagnosis and procedure outcomes data however does  
118 not include cancer stage or histology information. No ethical approval was required for this  
119 study. Patients or the public were not involved in the design, or conduct, or reporting of our  
120 research. The inclusion criteria for patients was a diagnosis of endometrial cancer (EC) or  
121 endometrial cancer in situ/complex atypical hyperplasia (ECIS) undergoing a hysterectomy  
122 between October 2011 to December 2017. The surgical approach was classified by intention-  
123 to-treat as open hysterectomy (OH), vaginal hysterectomy (VH), laparoscopic hysterectomy  
124 (LH), robotic hysterectomy (RH) and minimally invasive surgery (MIS) which was the  
125 combination of LH and RH. Due to the low numbers the VH cases were not included in any of  
126 the subsequent analyses. The cohort selection for the study has been described in more detail  
127 previously<sup>8</sup> and the list of specific diagnosis (ICD-10) and procedure (OPCS-4.7) codes can be  
128 found in the Appendix Table A1.

### 129 *Patient Characteristics*

130 Patient age was divided by 10-year intervals from the age of 50 into six groups. Ethnicity was  
131 classified into Asian, Black, Other and White. The Index of Multiple Deprivation (IMD) was  
132 split into statistical quartiles and indicated whether the sociodemographic status was high  
133 (>25083), intermediate (17475-25083), low (9618-17474) or very low (<9618) for each patient.  
134 Comorbidities were examined using the Charlson Comorbidity Index (CCI), an additional list  
135 of other co-morbidities were also assessed using specific ICD-10 codes (Appendix Table A2).

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3 136 Hospital characteristics were assessed by region (East, East Midlands, Greater London, Home  
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5 137 Counties, North East, North West, South East, South West, West Midlands, Yorkshire) and  
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8 138 volume, which was based on the annual mean of hysterectomies performed for EC/ECIS  
9  
10 139 grouped by statistical quartiles (High (>220), Intermediate (71-220), Low (70-21) and Very  
11  
12 140 Low (0-20)). MIS rates of hospitals for EC/ECIS hysterectomy procedures were classified into  
13  
14  
15 141 four groups based on percentage of hysterectomies performed by MIS approach (High (76-  
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17 142 100%), Intermediate (51-75%), Low (26-50%) and Very Low (0-25%)).

### 19 20 143 ***Outcomes***

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23 144 For each patient episode, in the HES database, a cost is assigned based on the health resource  
24  
25 145 group (HRG) which is diagnosis/procedure-based grouping and the length of stay. These costs  
26  
27 146 are based on reference costs provided by each hospitals and are estimated based upon recorded  
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29  
30 147 inpatient, outpatient, and A&E episode activity in the HES database using NHS Payment by  
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32 148 Results Health Resource Group (HRG) tariffs<sup>12</sup>. Costs were then summarised, by each  
33  
34 149 procedure approach, at intervention, 30 days, 90 days and 365 days. Further to this, the cost of  
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36 150 each approach was assessed by the subgroups of age, CCI groups and MIS rate classification.  
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39 151 A list of non-surgical cancer related treatments was collated (See Appendix Table A3 for  
40  
41 152 specific OPCS-4.7 procedure codes) and these costs were excluded in the analysis. Peri-  
42  
43 153 operative outcomes included mortality, conversion to open hysterectomy and length of stay.  
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46 154 The 90-day outcomes included the mortality, total and specific inpatient, outpatient and  
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48 155 emergency readmissions. Subgroup analyses were performed, firstly to assess high cost (top  
49  
50 156 5% of costs at intervention by approach) and low-cost patients (lowest 50% of costs at  
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52 157 intervention by approach) in the cohort to assess what was driving high costs patients. In  
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54 158 addition, provider level analysis was conducted to assess hospital characteristics and costs to  
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57 159 further understand the impact of differing MIS rates and volume sizes.  
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## 160 *Statistical Analyses*

161 A descriptive analysis of patient characteristics and data on costs and other health resource was  
162 performed. The different approaches (LH, RH, OH, MIS) were then compared by using t-test  
163 (for independent samples) and Wilcoxon rank-sum test (Mann-Whitney U test) for continuous  
164 variable and for categorical variables by using the chi-squared tests. The average marginal  
165 effect (AME)<sup>13</sup> was used to compare RH vs OH and RH vs LH on costing outcomes at  
166 intervention, 30 days, 90 days and 365 days. This approach adjusted for patient age, ethnicity,  
167 IMD rank, Charlson Comorbidity Index, year of procedure and whether a patient received  
168 cancer treatment following the intervention (for further details see Appendix Table A3) by  
169 fitting Generalised Linear Models (GLMS). The Modified Park Test & Pregibon's Link Test<sup>14</sup>  
170 were used to ensure the most efficient model structure was used to model the costs. All  
171 statistical analyses were performed using Stata 15®.

## 172 *Patient and Public Involvement*

173 There was no patient or public involvement in the study planning or design.

## 174 **RESULTS**

175 A total of 35,304 procedures were performed, 18,604 (52.7%) LH, 1,801 (5.1%) RH, 14,291  
176 (40.5%) OH and 608 (1.7%) VH. The proportion of MIS cases increased significantly overtime  
177 each year from 46.6% in 2012/13 to 68.7% in 2016/17 ( $p < 0.001$ ). This was primarily due to an  
178 increase in LH of 15.8% (44.7% to 60.5%), but there was also a 6.2% increase (2.0% to 8.2%)  
179 in the number of RH performed when comparing 2012/13 to 2016/17 as a proportion of all  
180 surgeries performed each year. Consequently, the number OH cases decreased significantly  
181 overtime ( $p < 0.001$ ) from 53.4% in 2012/13 to 31.3% in 2016/17 of cases in that year.

182 Table 1 presents the patient characteristics of the surgical approaches LH, RH and OH. Most  
183 cases were performed at high volume providers ( $>220$  cases/year) with 72.4% for RH, 62.1%

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3 184 for LH and 60.9% for OH being undertaken at these providers (Table 1). As previously  
4  
5 185 described, there was a significant difference in the social/racial characteristics of the women  
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7 186 undergoing MIS as compared to OH within this cohort of patients<sup>8</sup>. The characteristics of the  
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9 187 RH population differed to women undergoing LH; with a significantly higher percentage of  
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11 188 RH patients having any co-morbidity from our defined list than LH (68.2% vs 64.0%,  $p<0.001$ ),  
12  
13 189 more specifically the comorbidities of diabetes, hypertension and obesity all being higher  
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15 190 proportion in RH cohort than LH cohort.

### 191 ***Short-term costs by approach***

192 The short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach are  
193 presented in Table 2. LH was associated with the lowest mean cost at the intervention (£3069),  
194 30 (£3083), 90 (£3111) and 365 (£3169) days following the procedure. The mean cost for RH  
195 was significantly less than OH at all the time points ( $p<0.001$  for all). The average marginal  
196 effect (AME) for RH versus OH, controlling for patient characteristics, also showed a  
197 significant difference for RH over OH with the difference in cost increasing when comparing  
198 the unadjusted and AME value ( $p<0.001$  for all). Comparing RH and LH short-term costs, LH  
199 costs were significantly lower for the unadjusted and AME differences ( $p<0.001$  for all). The  
200 AME differences in cost between RH and LH were lower compared to the unadjusted  
201 differences (e.g., AME difference of £108 vs. unadjusted difference of £260 at intervention).

### 202 ***High-Cost and Low-Cost Patient Comparison***

203 Assessing the top 5% highest cost (HC) patients of each approach (LH:  $n=336$ ; OH:  $n=593$ ,  
204 RH:  $n=27$ ) and comparing to the low-cost (LC) cohort, which was set at less than or equal to  
205 the median cost of the surgery (LH:  $n=12,913$ ; OH:  $n=9,021$ , RH:  $n=812$ ). The patients in the  
206 HC group were significantly older in all the routes of surgery (LH: 69.0 vs 65.7 years, OH:  
207 68.8 vs 65.1 years, RH: 67.5 vs 65.5 years:  $p<0.001$  for all). The HC cohort contained a higher

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3 208 percentage of women from the lower socioeconomic groups (IMD Rank: 16637 vs 17287,  
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5 209  $p<0.001$ ) and women of non-white ethnicity (29.6% vs 19.2%,  $p<0.001$ ) as compared to the  
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7 210 LC cohort. Women in the HC cohort also had significantly greater number of co-morbidities  
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9 211 compared to the LC cohort (CCI 1.82 vs 1.41 and any comorbidity 71.0% versus 63.9%  
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11 212  $p<0.001$  for all). The length of hospital stay was significantly longer in the HC cases compared  
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13 213 to the LC group (RH: 11.22 vs 1.84 days; LH: 11.42 vs 2.03 days; OH: 20.82 vs 3.71days;  
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15 214  $p<0.001$  for all). Although the rate of complications was greater in the HC compared to the LC  
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17 215 cohort (RH: 55.6% vs 14.0%; LH: 61.0% vs 16.2%; OH: 71.5% vs 19.1%;  $p<0.001$  for all),  
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19 216 the rate was significantly lower with RH as compared to OH in both the HC and LC groups  
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21 217 (HC: 55.6% vs 71.5%,  $p=0.075$ ; LC: 14.0% vs 19.1%,  $p<0.001$ ).

### 27 218 ***Patient Characteristics and Costs***

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29 219 Patient characteristics, age and CCI, were associated with increasing costs for almost all routes  
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31 220 of surgery at intervention, and 365 days following the procedure (Table 3). Assessing the age  
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33 221 categories showed the costs at intervention were very similar for the <50 years, 50-59 years  
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35 222 and 60-69 years groups but gradually increased for each of the higher age groups. There was  
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37 223 an increasing difference between the MIS and OH costs with rising age with the difference  
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39 224 between MIS and OH for Age <50 being £258 increasing to a difference of £653 for Age >90  
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41 225 years population. RH costs were significantly lower ( $p<0.001$ ) than OH in all age categories  
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43 226 except 60-69 years. Comparing CCI showed that CCI group  $\geq 3$  was associated with the  
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45 227 greatest difference in costs with the difference at 365 days between CCI group 1 and CCI group  
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47 228  $>3$  being £130 for RH, £174 for LH and £759 for OH (Table 3).

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49 229 Overtime patients who underwent RH became increasingly complex, when using the CCI  
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51 230 score, and have in recent years had a higher average CCI than LH in 2015/16-2016/17 (Figure  
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53 231 1). Comparing the cost of LH and RH against CCI score, identified that the costs closely

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3 232 reflected the patients' CCI. In 2012/13 when the RH population had a lower CCI then the costs  
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5 233 were less, however, since 2014/15 the patient population undergoing RH higher CCI score and  
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7 234 this was associated with a rise in the costs of RH above that of LH (Figure 1).  
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### 10 235 *Hospital Characteristics and Costs*

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13 236 When exploring the association between provider volume, MIS rate and surgical costs there  
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15 237 was an association with the MIS rate and cost, i.e. the greater the MIS rate the lower the cost  
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17 238 (Figure 2). Many of the highest volume providers had higher average costs than providers with  
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19 239 less volume, however the patient population undergoing surgery at the high volume providers  
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21 240 were significantly older and had a higher CCI compared to the lower volume providers (Age:  
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23 241 66.2 vs 65.6 years,  $p<0.001$ ; CCI: 1.47 vs 1.43,  $p<0.001$ ). The majority of the highest volume  
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25 242 providers had MIS rates between 50% to 90% and the relationship held for high volume  
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27 243 providers with average costs decreasing as MIS rates increased for the year 2016/17.  
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## 32 244 **DISCUSSION**

### 33 245 *Main findings*

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36 246 In this study, we have performed an in-depth analysis of real-world data and have identified  
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38 247 financial benefits for MIS as compared to OH for EC. We have demonstrated that LH has the  
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40 248 lowest mean cost at intervention and that costs increased with increasing patient age. In keeping  
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42 249 with other studies, we have also shown that OH, although attracting the lowest operative  
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44 250 consumable costs, had the greatest overall financial cost, even significantly higher than RH.  
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46 251 We have also identified that patients undergoing RH have different characteristics compared  
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48 252 to women having LH in recent years, and that cost of surgery appears to be influenced by level  
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50 253 of patients' co-morbidities rather than the route of surgery alone.  
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58 254 There will always be a proportion of cases that have to be performed OH due to contra-  
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60 255 indications/complications with MIS, which will inevitably attract higher costs due to their

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3 256 complexity, but this can be reduced to low levels<sup>15</sup>. The longer recovery time and significantly  
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5 257 higher complication/re-admission rate with OH may impact on patient and employment costs,  
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8 258 with greater loss of earnings and longer return to work or contribution to society activities as  
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10 259 compared to MIS. Korsholm et al.<sup>16</sup>, reported no significant difference in return to the labour  
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12 260 market or use of sickness benefits in a study from Denmark however, in their study robotic  
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14 261 surgery was associated with greater cost than both laparoscopic and open hysterectomy, unlike  
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16 262 this UK analysis. Allowing for a number of OH cases, the disparity in MIS uptake across  
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18 263 England<sup>8</sup> does indicate that there is room for improvement in increasing the proportion of MIS  
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20 264 cases and thereby benefitting both the patient and the healthcare economy.  
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24 265 The primary argument used against the widespread use of RH, rather than LH, for EC is an  
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26 266 economic one<sup>6,17</sup>, since the clinical outcomes are comparable although, there is a lack of  
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28 267 randomised control trial data, particular for high BMI patients<sup>18</sup>. The HES data does confirm a  
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30 268 cost advantage for LH over RH however, the two patient populations are not directly  
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32 269 comparable since there is a significant difference in the CCIs between the groups. During  
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34 270 2012/13, when RH was only performed in a few selected centres, the majority of UK robotic  
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36 271 surgeons would still have been within the learning phase, and therefore likely to select patients  
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38 272 with less co-morbidities for RH. We have shown that during this time period the cost of RH  
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40 273 was less than LH. Increasing robotics experience appears to have led to the positive selection  
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42 274 of co-morbid patients, especially obesity, for RH, and this is associated with rising costs. Class  
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44 275 III obesity and rising number of patient co-morbidities are reported to attract increased inpatient  
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46 276 care costs due to increased medical rather than surgical complications associated with  
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48 277 undergoing surgery<sup>19,20</sup>. The selection of high-BMI cases for RH is not unexpected given the  
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50 278 reported ergonomic benefits for surgeons as compared to straight-stick laparoscopy<sup>21</sup>, with less  
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52 279 movements and muscle activity required to perform tasks<sup>22</sup>. RH is not without issues due to the  
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54 280 fixed console position<sup>23</sup>, however more extreme muscle movements are required for  
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3 281 laparoscopic procedures increase with rising BMI<sup>22</sup>, which is not reported with robotics. The  
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5 282 cost to the healthcare service of work-related musculoskeletal symptoms in surgeons is of  
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8 283 growing concern<sup>24</sup> and not considered in economic analyses such as this study, however it is  
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10 284 an additional cost that needs to be considered when calculating service delivery costs.

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13 285 What is clear the data is that OH is the most costly route of surgery, a finding reported in other  
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15 286 healthcare settings<sup>25</sup>, not only in financial terms but more importantly for patient complications  
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17 287 and post-operative mortality<sup>8</sup>. The key focus therefore, rather than being between LH or RH,  
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19 288 should instead be on reducing the OH rate to a minimum. Although there are only a few  
20  
21 289 absolute contra-indications for OH, the number of cases that are performed through open  
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23 290 surgery is still high in some institutions and there has been much discussion how this could be  
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25 291 reduced through greater surgical training<sup>26</sup> or centralisation of cases to hospitals and surgeons  
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27 292 with high MIS rates<sup>27</sup>. A reduction in OH can also be achieved through reducing the number  
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29 293 of conversions from LH/RH to a minimum. A meta-analysis of observational studies did show  
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31 294 that the conversion rate of LH increased with BMI >40kg/m<sup>2</sup> more than for RH, 6.5% (95% CI  
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33 295 4.3-9.9) versus 5.5% (95% CI 3.3-9.1), as compared to >30kg/m<sup>2</sup>, 7.0% (95% CI 3.2-14.5)  
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35 296 versus 3.8% (95% CI 1.4-9.9) respectively<sup>18</sup>. One reason for this may be the lower intra-  
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37 297 abdominal insufflation pressure used with RH, typically 8mmHg, which has been shown to be  
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39 298 associated with lower post-operative pain and shorter hospital stay as compared to standard  
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41 299 pressure (15mmHg)<sup>28</sup>. Inability to tolerate Trendelenburg position was reported to be the  
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43 300 indication for 31% of LH conversions but only 6% of RH conversions<sup>18</sup>. This therefore raises  
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45 301 the possibility as to whether cases should be selected for RH where there is high risk of  
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47 302 conversion due to severe obesity or inability tolerate the pneumoperitoneum.  
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55 303 ***Strengths and limitations***  
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3 304 The key strength of the study is in the number of patients in which can be analysed by using  
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5 305 the HES database. This gives strength to the study's findings as it is representative of all  
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7 306 procedures via the NHS in England. Due to RH being a newer surgery approach the number of  
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9 307 patients is much lower compared to the other surgery approaches. In addition, we must consider  
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11 308 the impact of a learning curve of RH and that in the earlier years it may not been used to full  
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13 309 efficiency. As we had a number of years of the HES database we could analyse any potential  
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15 310 trends across surgical approaches and the year.

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20 311 As we have previously described<sup>8</sup>, HES data does have limitations primarily it only covered  
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22 312 NHS-funded care, the reliability of coding and lacks oncological details of stage/histology.  
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24 313 There will be a proportion of patients with advanced disease that require open surgery due to  
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26 314 requiring a more extensive cytoreductive procedure and HES data is not able to differentiate  
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28 315 these cases from early stage disease that is being treated through open surgery. The analysis  
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30 316 comparing LH and RH should however not be impacted by stage of disease.

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34 317 The capital and maintenance costs of RH have also not been included since these costs vary  
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36 318 dramatically across different healthcare settings and there would be a need to also included  
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38 319 similar costs for laparoscopic and open surgery. In addition, the robotic surgery equipment is  
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40 320 often utilised by a wide group of specialities in a hospital setting and it would be infeasible to  
41  
42 321 apply capital and maintenance costs to one surgery modality<sup>13</sup>.

### 322 ***Interpretation***

323 In conclusion, LH was associated with the lowest and OH the greatest mean cost per procedure.  
324 Patient factors have an impact on the cost of MIS procedures and further research is needed to  
325 compare the costs in matched populations of women undergoing LH and RH, since there  
326 appears to be selection bias in the choice of procedure being performed.

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3 327 **Ethical approval:** The HES database is managed by the NHS Digital and is available for  
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5 328 research without ethical approval.  
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9 330 All the authors consent to publication  
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13 332 **Data availability:** Data analysed in this study is available through Hospital Episode Statistics  
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16 333 (HES)  
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18  
19 334 **Conflicts of Interest:** EM and TI perform Da’Vinci robotic gynaecological surgery (Intuitive  
20  
21 335 Surgical) and are members of the British and Irish Association of Robotic Surgeons (BIARGS),  
22  
23 336 which is supported by Intuitive Surgical and other robotics/laparoscopic companies to hold  
24  
25 337 education/training events. EM has been awarded research grants from Intuitive Surgical and  
26  
27 338 Hope Against Cancer for unrelated studies. TI has done two days paid consultancy work for  
28  
29 339 Medtronic. GM and AM from HCD Economics were funded by Intuitive Surgical. None of the  
30  
31 340 clinicians (EM, PS, TI) received funding from Intuitive Surgical for this study. Intuitive  
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33 341 Surgical did not have any involvement with the study design, data analysis and writing of the  
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35 342 manuscript. The authors declare no other potential conflict of interest.  
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43 344 **Contributors:** EM, TI, GM and AM contributed to the conceptualisation and study design.  
44  
45 345 Data analysis and interpretation was performed by EM, TI, GM, AM and PS. Figures and tables  
46  
47 346 creation was performed by EM, GM and AM. All authors were involved in the writing or  
48  
49 347 review of the manuscript and approved the final version.  
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54  
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56  
57 350 & Social Care Information Centre 2018.  
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3 351 **Figure 1: Intervention Cost & CCI Over Time**  
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5 352 The average cost and CCI of RH & LH over time.

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7 353 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic  
8 354 hysterectomy, NHS = National Health Service)  
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10 355 **Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17**

11 356 The association between provider volume, MIS rate and surgical cost at intervention. Provider  
12 357 volume is represented by the size of the bubble with a larger bubble representing a higher  
13 358 provider volume.  
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465 **Table 1. Clinical and Demographic Characteristics by the cohorts of hysterectomy approach**

Characteristics	Unadjusted Results							
	Laparoscopic Hysterectomy (N=18604)		Robotic Hysterectomy (N=1801)		MIS Hysterectomy (N=20405)		Open Hysterectomy (N=14291)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<b>NHS Year of surgery</b>								
2011/12*	1,108	6%	19	1%	1,127	6%	1,671	12%
2012/13	2,367	13%	104	6%	2,471	12%	2,829	20%
2013/14	2,824	15%	147	8%	2,971	15%	2,614	18%
2014/15	3,134	17%	253	14%	3,387	17%	2,361	17%
2015/16	3,118	17%	382	21%	3,500	17%	1,948	14%
2016/17	3,577	19%	483	27%	4,060	20%	1,852	13%
2017/18*	2,476	13%	413	23%	2,889	14%	1,016	7%
<b>Age, years</b>								
<50	1,033	6%	120	7%	1,153	6%	1,082	8%
50-59	3,937	21%	380	21%	4,317	21%	3,098	22%
60-69	6,522	35%	589	33%	7,111	35%	4,672	33%
70-79	5,160	28%	533	30%	5,693	28%	3,779	26%
80-89	1,846	10%	174	10%	2,020	10%	1,540	11%
90>	106	1%	5	0%	111	1%	120	1%
<b>Ethnicity</b>								
White	15,033	81%	1,420	79%	16,453	81%	11,117	78%
Asian	583	3%	66	4%	649	3%	499	3%
Black	231	1%	20	1%	251	1%	365	3%
Other	2,757	15%	295	16%	3,052	15%	2,310	16%
<b>Socio-Economic Group (IMD)</b>								

High	4,506	25%	643	37%	5,149	25%	3,291	23%
Intermediate	4,612	25%	403	23%	5,015	25%	3,387	24%
Low	4,548	25%	376	21%	4,924	24%	3,489	24%
Very Low	4,435	25%	333	19%	4,768	23%	3,703	26%
<b>Charlson Comorbidity Group</b>								
0	22	0%	1	0%	23	0%	13	0%
1	12,432	67%	1,159	64%	13,591	67%	8,405	59%
2	4,915	26%	514	29%	5,429	27%	4,535	32%
>=3	1,235	7%	127	7%	1,362	7%	1,338	9%
<b>Region</b>								
Greater London	2,529	14%	319	18%	2,848	14%	2,184	15%
Yorkshire	1,501	8%	270	15%	1,771	9%	1,220	9%
West Midlands	1,747	9%	154	9%	1,901	9%	1,672	12%
South West	2,676	14%	75	4%	2,751	13%	1,348	9%
South East	1,746	9%	339	19%	2,085	10%	1,451	10%
North West	2,628	14%	281	16%	2,909	14%	2,550	18%
North East	1,264	7%	138	8%	1,402	7%	432	3%
Home Counties	1,095	6%	31	2%	1,126	6%	912	6%
East Midlands	1,485	8%	165	9%	1,650	8%	1,003	7%
East	1,922	10%	4	0%	1,926	9%	1,497	10%
<i>Missing</i>	11	0%	25	1%	36	0%	22	0%
<b>Provider Volume</b>								
High	11,423	62%	1,302	72%	12,725	62%	8,703	61%
Intermediate	6,653	36%	487	27%	7,140	35%	5,102	36%
Low	279	2%	9	1%	288	1%	191	1%
Very Low	36	0%	0	0%	36	0%	58	0%
<i>Missing</i>	213	1%	3	0%	216	1%	237	2%

\*NHS Year 2011/12 & 2017/18 not full year

468 **Table 2. Short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach**

	Mean Cost in £ (SD)			Difference RH vs OH				Difference RH vs LH			
	RH (N =1353)	OH (N=12379)	LH (N=15666)	Unadjusted Difference (£)	P Value	AME (£) *	P Value	Unadjusted Difference (£)	P Value	AME (£) *	P Value
<b>At Intervention</b>	3329 (713)	3349 (1318)	3069 (676)	-20	<0.001	-197	<0.001	260	<0.001	108	<0.001
<b>At 30 days</b>	3334 (722)	3379 (1395)	3083 (721)	-45	<0.001	-220	<0.001	251	<0.001	98	<0.001
<b>At 90 days</b>	3357 (761)	3424 (1468)	3111 (826)	-67	<0.001	-241	<0.001	246	<0.001	89	<0.001
<b>At 365 days</b>	3417 (906)	3533 (1687)	3169 (984)	-116	<0.001	-273	<0.001	248	<0.001	94	<0.001

469 \*AME adjusted for Year, Age, Socioeconomic Status (IMD Rank), Charlson Comorbidity, Ethnicity, Cancer Tx

470 Notes:

471 RH vs OH: We see that the average marginal effect is greater than the actual difference between RH and OH when we control for covariates

472 RH vs LH: We see the average marginal effect is less than the actual difference between RH and LH when we control for covariates

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6/bmjopen-2020-045888 on 13 May 2021. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



480 **Table 3. Mean Cost at intervention and 365 days by CCI/Age for each approach**

	LH		RH		MIS		OH	
	N	Cost	N	Cost	N	Cost	N	Cost
<b>Intervention</b>								
<i>Age Groups</i>								
<50	860	£ 3,031.89	90	£ 3,283.71	950	£ 3,055.74	921	£ 3,313.62
50-59	3336	£ 3,024.86	293	£ 3,257.56	3629	£ 3,043.65	2687	£ 3,259.23
60-69	5522	£ 3,052.62	436	£ 3,356.87	5958	£ 3,074.89	4077	£ 3,283.08
70-79	4328	£ 3,101.11	398	£ 3,343.10	4726	£ 3,121.49	3255	£ 3,418.83
80-89	1533	£ 3,148.51	134	£ 3,385.03	1667	£ 3,167.52	1338	£ 3,546.07
90>	87	£ 3,214.70	<10	£ 3,453.50	89	£ 3,220.07	101	£ 3,855.14
<i>CCI Groups</i>								
0	21	£ 3,060.48	<10	£ 3,939.00	22	£ 3,100.41	12	£ 2,968.00
1	10526	£ 3,038.06	887	£ 3,319.27	11413	£ 3,059.92	7369	£ 3,246.57
2	4126	£ 3,125.58	377	£ 3,337.09	4503	£ 3,143.29	3875	£ 3,411.77
>=3	993	£ 3,166.00	88	£ 3,391.30	1081	£ 3,184.30	1123	£ 3,808.20
<b>365 days</b>								
<i>Age Groups</i>								
<50	860	£ 3,136.11	90	£ 3,286.98	950	£ 3,150.40	921	£ 3,614.82
50-59	3336	£ 3,111.41	293	£ 3,273.97	3629	£ 3,124.53	2687	£ 3,398.50
60-69	5522	£ 3,144.29	436	£ 3,475.53	5958	£ 3,168.53	4077	£ 3,448.76
70-79	4328	£ 3,219.07	398	£ 3,467.83	4726	£ 3,240.02	3255	£ 3,606.54
80-89	1533	£ 3,256.01	134	£ 3,476.81	1667	£ 3,273.76	1338	£ 3,776.23
90>	87	£ 3,252.47	<10	£ 3,453.50	89	£ 3,256.99	101	£ 4,174.64
<i>CCI Groups</i>								
0	21	£ 3,074.48	<10	£ 3,939.00	22	£ 3,113.77	12	£ 2,968.00
1	10526	£ 3,125.62	887	£ 3,358.03	11413	£ 3,143.68	7369	£ 3,389.67
2	4126	£ 3,248.94	377	£ 3,538.35	4503	£ 3,273.17	3875	£ 3,629.09
>=3	993	£ 3,299.13	88	£ 3,488.25	1081	£ 3,314.52	1123	£ 4,148.06

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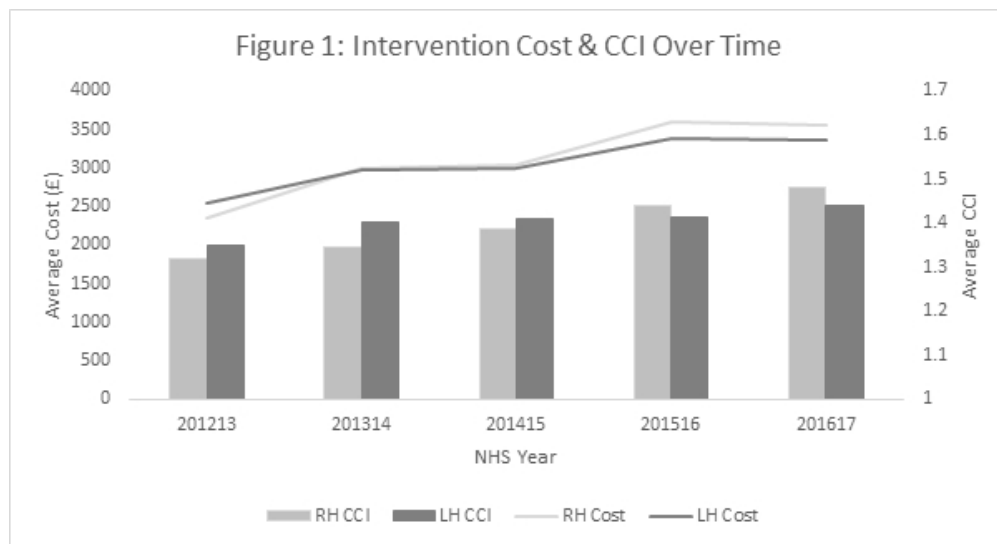


Figure 1: Intervention Cost & CCI Over Time  
 The average cost and CCI of RH & LH over time.  
 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic hysterectomy, NHS = National Health Service)

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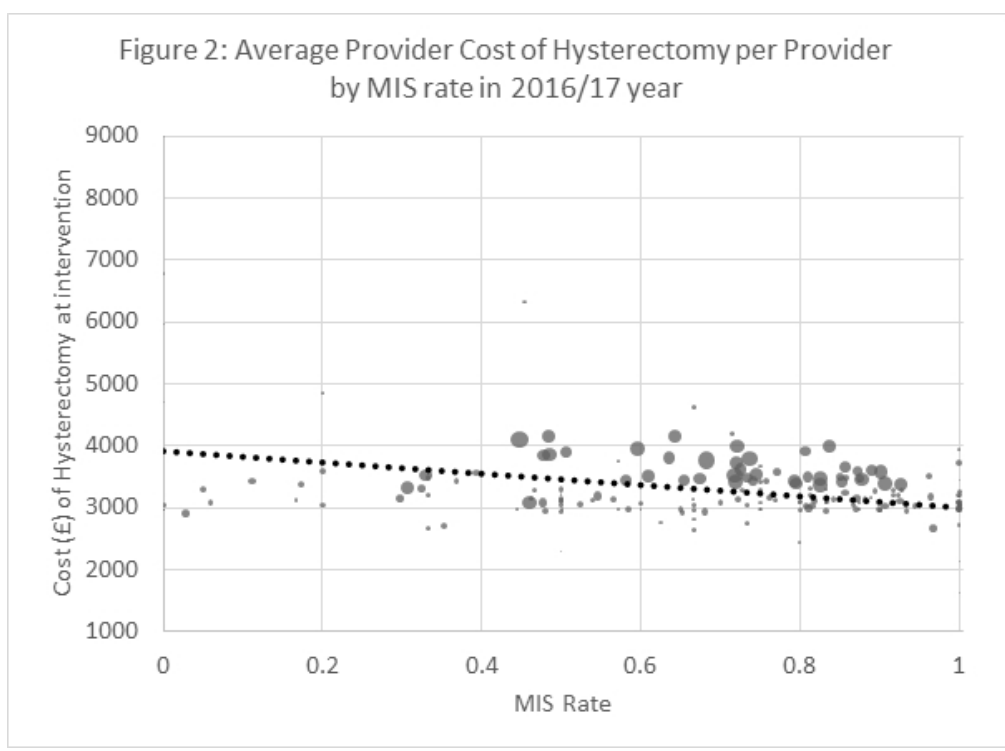


Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17  
 The association between provider volume, MIS rate and surgical cost at intervention. Provider volume is represented by the size of the bubble with a larger bubble representing a higher provider volume.

127x93mm (120 x 120 DPI)

## Appendix Tables:

Table A1- Cohort Selection ICD-10 & OPCS-4.7 Codes

**Table A1: Cohort Selection**

Category	ICD-10 / OPCS-4.7
<b>Hysterectomies</b>	Procedures with: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9
<b>Endometrial/uterine carcinoma or endometrial carcinoma in situ</b>	Patients must have as primary diagnosis: C540, C541, C542, C543, C548, C549, C55X, D070
<b>Laparoscopic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9
<b>Robotic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.3
<b>Open hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Vaginal hysterectomy</b>	Any procedures with one of: Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Minimally Invasive Surgery</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9, Y75.3

Table A2 – Other complications OPCS-4.7 codes assessed

Table A2: Complication classification<sup>a</sup>

Category	ICD-10 / OPCS-4.7
<b>Gastrointestinal complications</b>	A090 I898 K228 K250 K252 K254 K256 K260 K261 K262 K264 K265 K266 K270 K272 K274 K276 K280 K282 K284 K286 K290 K450 K560 K565 K566 K567 K625 K631 K638 K660 K720 K729 K85 K913 K918 K919 K92 S360 K61 N824
<b>Wounds</b>	D649 K603 K604 K605 K632 K829 K832 L89 T813 T815 T343 T453 T793
<b>Infections</b>	A40 A41 A49 B95 B96 K630 K65 L03 L04 N10 N12 N151 N159 N300 N309 N390 R788 T793 T802 T814 T816 T827 T836 T857
<b>Uteric Injury Complication</b>	N133 N139 N17 N19 N280 N312 N990 N991 N998 N999 R32 R33 S360 N12 N151 N159 N300 N309 N390 N360 S371 N131 N821
<b>Haemorrhage</b>	T810 S35 D65
<b>Cardiovascular disorders</b>	I21 I46 I48 I49 I50 I74 I80 I81 I82 I950 I952 I959 I978 I979 R57 T801 T811 T817 T827
<b>Pulmonary complications</b>	J80 J81 J90 J91 J93 J955 J958 J959 J960 J969 J981 R060 R09 I26 J100 J110 J12 J13 J14 J15 J16 J17 J18 J690 J85 J86
<b>Neurological disorders</b>	F05 F13 F15 F19 G45 G46 G569 G81 G82 G83 G931 G936 G970 G971 G978 G979 I63 I65
<b>Other</b>	T882 T790 T800 E15 E272 E86 E87 R798 T812 T818 T888 T792

<sup>a</sup> Adapted from Ma C, et al. Postoperative complications following colectomy for ulcerative colitis: A validation study. BMC Gastroenterol 2012; 12:39.

Table A3: Cancer Treatment OPCS 4.7 Codes excluded for cost analysis

Category	Specific Code	Sub Category
Chemotherapy	X70.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 1
	X70.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 2
	X70.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 3
	X70.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 4
	X70.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 5
	X70.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X70.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X71.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 6
	X71.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 7
	X71.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 8
	X71.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 9
	X71.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 10
	X71.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X71.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X72.1	Delivery of complex chemotherapy for neoplasm including prolonged infusional treatment at first attendance
	X72.2	Delivery of complex parenteral chemotherapy for neoplasm at first attendance
	X72.3	Delivery of simple parenteral chemotherapy for neoplasm at first attendance
	X72.4	Delivery of subsequent element of cycle of chemotherapy for neoplasm
	X72.8	Other specified delivery of chemotherapy for neoplasm
	X72.9	Unspecified delivery of chemotherapy for neoplasm
	X73.1	Delivery of exclusively oral chemotherapy for neoplasm
	X73.8	Other specified delivery of oral chemotherapy for neoplasm
	X73.9	Unspecified delivery of oral chemotherapy for neoplasm
	X74.1	Cancer hormonal treatment drugs Band 1
	X74.2	Cancer supportive drugs Band 1
	X74.8	Other specified other chemotherapy drugs
	X74.9	Unspecified other chemotherapy drugs
	Radiotherapy	X65.1
X65.2		Delivery of a fraction of intracavitary radiotherapy
X65.3		Delivery of a fraction of interstitial radiotherapy
X65.4		Delivery of a fraction of external beam radiotherapy NEC
X65.5		Oral delivery of radiotherapy for thyroid ablation
X65.6		Delivery of a fraction of intraluminal brachytherapy
X65.7		Delivery of radionuclide therapy NEC
X65.8		Other specified radiotherapy delivery
X65.9		Unspecified radiotherapy delivery
X67.1		Preparation for intensity modulated radiation therapy
X67.2		Preparation for total body irradiation
X67.3		Preparation for hemi body irradiation
X67.4		Preparation for simple radiotherapy with imaging and dosimetry
X67.5		Preparation for simple radiotherapy with imaging and simple calculation
X67.6		Preparation for superficial radiotherapy with simple calculation
X67.7		Preparation for complex conformal radiotherapy
X67.8	Other specified preparation for external beam radiotherapy	

	X67.9	Unspecified preparation for external beam radiotherapy
	Y92.1	Technical support for preparation for radiotherapy
	Y92.2	Other specified support for preparation for radiotherapy
	Y92.3	Unspecified support for preparation for radiotherapy
Brachytherapy	X68.1	Preparation for intraluminal brachytherapy
	X68.2	Preparation for intracavitary brachytherapy
	X68.3	Preparation for interstitial brachytherapy
	X68.8	Other specified preparation for brachytherapy
	X68.9	Unspecified preparation for brachytherapy
	Y35.4	Introduction of radioactive substance into organ for brachytherapy NOC
	Y36.4	Introduction of non-removable radioactive substance into organ for brachytherapy NOC
	Y89.1	High dose rate brachytherapy treatment
	Y89.2	Pulsed dose rate brachytherapy treatment
	Y89.8	Other specified brachytherapy
	Y89.9	Unspecified brachytherapy

# BMJ Open

## Economic evaluation of different routes of surgery for the management of endometrial cancer: A retrospective cohort study.

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Secondary Subject Heading:	Obstetrics and gynaecology, Oncology
Keywords:	SURGERY, Minimally invasive surgery < GYNAECOLOGY, Gynaecological oncology < GYNAECOLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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3 **1 Economic evaluation of different routes of surgery for the management of endometrial**  
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5 **2 cancer: A retrospective cohort study.**  
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20 **Word count: 3575**  
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22

1  
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3 23 **ABSTRACT**  
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6 24 **Objectives:** The benefits of minimally invasive surgery (MIS) for endometrial carcinoma (EC)  
7  
8 25 are well established although the financial impact of robotic-assisted hysterectomy (RH)  
9  
10 26 compared to laparoscopic hysterectomy (LH) is disputed.

11  
12  
13 27 **Design:** Retrospective cohort study.

14  
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16 28 **Setting:** English NHS hospitals 2011-2017/8.

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18  
19 29 **Participants:** 35,304 women having a hysterectomy for EC identified from Hospital Episode  
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21  
22 30 Statistics (HES).

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24  
25 31 **Primary and secondary outcome measures:** The primary outcome was the association  
26  
27 32 between route of surgery on cost at intervention, 30, 90 and 365 days for women undergoing  
28  
29 33 an open (OH) or MIS (LH/RH) for EC in England. The average marginal effect (AME) was  
30  
31 34 calculated to compare RH vs OH/RH vs LH which adjusted for any differences in the  
32  
33 35 characteristics of the surgical approaches. Secondary outcomes were to analyse costing data  
34  
35 36 for each surgical approach by age, Charlson Comorbidity Index (CCI) and hospital MIS rate  
36  
37 37 classification.

38  
39 38 **Results:** A total of 35,304 procedures were performed, 20,405 (57.8%) were MIS (LH 18,604  
40  
41 39 and RH 1,801), 14,291 (40.5%) OH. Mean cost for LH was significantly less than RH, whereas  
42  
43 40 RH was significantly less than OH at intervention, 30, 90 and 365 days ( $p < 0.001$ ). Overtime  
44  
45 41 patients who underwent RH had increasing CCI scores and by the 2015/16 year had a higher  
46  
47 42 average CCI than LH. Comparing the cost of LH and RH against CCI score identified that the  
48  
49 43 costs closely reflected the patients' CCI. Increasing disparity was also seen between the MIS  
50  
51 44 and OH costs with rising age. When exploring the association between provider volume, MIS  
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53 45 rate and surgical costs there was an association with the higher the MIS rate the lower the  
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55 46 average cost.  
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3 47 **Conclusions:** Further research is needed to investigate costs in matched populations to  
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6 48 determine optimum surgical modality in different populations.  
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14 51 **Funding:** HCD economics were funded by Intuitive Surgical, Award/Grant number is not  
15  
16 52 applicable. None of the clinicians involved in this study received funding from Intuitive  
17  
18 53 Surgical. Intuitive Surgical did not have any involvement with the study design, data analysis  
19  
20 54 or writing of the manuscript.  
21  
22  
23

24 55 **Key words:** Endometrial cancer; minimally invasive surgery; laparoscopic hysterectomy; open  
25  
26 56 hysterectomy; robotic-assisted hysterectomy; patient stratification; healthcare economy  
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32 58 **Tweetable abstract:** Analysis of financial cost of laparoscopic, robotic and open hysterectomy  
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34 59 for the treatment of endometrial cancer in England.  
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3 68 ***Strengths and limitations***  
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- 6 69 • The findings from the study are based on a population-based database which is a key  
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8 70 strength as it is representative of all procedures via the NHS in England.  
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10  
11 71 • The reliability of the coding might have changed over time although there was no  
12  
13 72 evidence of changes in treatment coding or significant changes in the underlying study  
14  
15 73 population.  
16  
17  
18 74 • HES database reliably captures extensive amount of demographic, diagnosis and  
19  
20 75 procedure outcomes however there is a lack of cancer stage information therefore it is  
21  
22 76 not possible to split out the cost outcomes into more specific groups of patients.  
23  
24  
25 77 • The capital and maintenance costs of RH have also not been included since these costs  
26  
27 78 vary dramatically across different healthcare settings and often utilised by a wide group  
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29 79 of specialities in a hospital setting.  
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31  
32 80 • As the analysis was undertaken over a number of years of the HES database, we were  
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34 81 able to accurately follow hospital activity for at least a year after intervention.  
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## 90 INTRODUCTION

91 The introduction of minimally invasive surgery (MIS) for endometrial cancer (EC) has had a  
92 dramatic impact on patients' surgical outcomes with reduced morbidity, hospital stay and  
93 improved short-term quality of life<sup>1</sup>. Translating these patient benefits into cost benefits to the  
94 healthcare economy has been challenging because although MIS requires significantly less bed  
95 days than open surgery, it does require more costly consumable equipment, for example single-  
96 use vessel sealing devices. This has been demonstrated in several studies including the multi-  
97 centre randomised LACE trial where the surgery costs were greater for laparoscopic  
98 hysterectomy (LH) compared to open hysterectomy (OH), but the overall costs of treatment  
99 were lower<sup>2</sup>.

100 MIS is the preferred surgical route for EC<sup>3</sup>. RH is accepted as an alternative to LH, supported  
101 by evidence from a randomised controlled trial<sup>4</sup> and RH has been shown to have a lower  
102 conversion rate to laparotomy and shorter operating time<sup>5-7</sup>. Wide spread adoption of RH is  
103 limited in England, although the number of EC cases having RH is increasing year on year<sup>8</sup>. In  
104 light of the capital and consumable costs of RH, as compared to OH or LH, the use of RH in  
105 EC is therefore being called into question<sup>6</sup>. Reports from institutions with well-established  
106 robotic programmes however have contested this view with no significant difference<sup>9</sup>, or cost  
107 improvements reported as compared to LH<sup>10</sup>. What is clear is that focusing solely on in-hospital  
108 costs does not give the full picture of the economic costs of a surgical procedure, since many  
109 costs are accrued following discharge or attributed to the economy as a whole as a result of  
110 delayed return to employment.

111 We therefore investigated the HES data for England in order to look at the financial impact of  
112 RH as compared to LH and OH. We also investigated the patient characteristics that contributed

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3 113 to cost and examined the top 5% of procedures to identify factors that may have contributed to  
4  
5 114 the costs.

## 8 115 **METHODS**

### 11 116 *Data Source and cohort selection*

13  
14 117 Data was sourced from the Hospital Episode Statistics (HES) database from 2011-2017/8<sup>11</sup>.  
15  
16 118 HES database captures demographic, diagnosis and procedure outcomes data however does  
17  
18 119 not include cancer stage or histology information. No ethical approval was required for this  
19  
20 120 study. Patients or the public were not involved in the design, or conduct, or reporting of our  
21  
22 121 research. The inclusion criteria for patients was a diagnosis of endometrial cancer (EC) or  
23  
24 122 endometrial cancer in situ/complex atypical hyperplasia (ECIS) undergoing a hysterectomy  
25  
26 123 between October 2011 to December 2017. The surgical approach was classified by intention-  
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28 124 to-treat as open hysterectomy (OH), vaginal hysterectomy (VH), laparoscopic hysterectomy  
29  
30 125 (LH), robotic hysterectomy (RH) and minimally invasive surgery (MIS) which was the  
31  
32 126 combination of LH and RH. Due to the low numbers the VH cases were not included in any of  
33  
34 127 the subsequent analyses. The cohort selection for the study has been described in more detail  
35  
36 128 previously<sup>8</sup> and the list of specific diagnosis (ICD-10) and procedure (OPCS-4.7) codes can be  
37  
38 129 found in the Appendix Table A1.

### 45 130 *Patient Characteristics*

46  
47  
48 131 Demographic data was captured in the hospital admission data for each patient and included  
49  
50 132 age, ethnicity, postcode, comorbidities. Patient age was divided by 10-year intervals from the  
51  
52 133 age of 50 into six groups. Ethnicity was classified into Asian, Black, Other and White. Based  
53  
54 134 on postcode of residence, each patient who received EC surgery was mapped to the English  
55  
56 135 Index of Multiple Deprivation rank. The IMD indicates the socioeconomic deprivation of  
57  
58 136 patients which combines seven indicators (income, employment, health deprivation and  
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3 137 disability, education, skills and training, barriers to housing and services, crime, and living  
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5 138 environment), into a single deprivation index where a higher rank indicated a less deprived  
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8 139 group and a lower rank indicated a more deprived group<sup>12</sup>. The Index of Multiple Deprivation  
9  
10 140 (IMD) was split into statistical quartiles and indicated whether the sociodemographic status  
11  
12 141 was high (>25083), intermediate (17475-25083), low (9618-17474) or very low (<9618) for  
13  
14 142 each patient. Comorbidities were examined 12 months prior to intervention using the Charlson  
15  
16 143 Comorbidity Index (CCI)<sup>13</sup>, an additional list of other co-morbidities were also assessed using  
17  
18 144 specific ICD-10 codes (Appendix Table A2).

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20  
21  
22 145 Hospital characteristics were assessed by region (East, East Midlands, Greater London, Home  
23  
24 146 Counties, North East, North West, South East, South West, West Midlands, Yorkshire) and  
25  
26  
27 147 volume, which was based on the annual mean of hysterectomies performed for EC/ECIS  
28  
29 148 grouped by statistical quartiles (High (>220), Intermediate (71-220), Low (70-21) and Very  
30  
31 149 Low (0-20)). MIS rates of hospitals for EC/ECIS hysterectomy procedures were classified into  
32  
33 150 four groups based on percentage of hysterectomies performed by MIS approach (High (76-  
34  
35 151 100%), Intermediate (51-75%), Low (26-50%) and Very Low (0-25%)).

### 38 39 152 ***Outcomes***

40  
41  
42 153 For each patient episode, in the HES database, a cost is assigned based on the health resource  
43  
44 154 group (HRG) which is diagnosis/procedure-based grouping and the length of stay. These costs  
45  
46 155 are based on reference costs provided by each hospitals and are estimated based upon recorded  
47  
48 156 inpatient, outpatient, and A&E episode activity in the HES database using NHS Payment by  
49  
50 157 Results Health Resource Group (HRG) tariffs<sup>14</sup>. Costs at intervention and short-term costs were  
51  
52 158 calculated based upon the reported hospital admission costs over the time period of 30-, 90-  
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54 159 and 365-days following intervention, these were all summarised by procedure approach.  
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57 160 Further to this, the cost of each approach was assessed by the subgroups of age, CCI groups  
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3 161 and MIS rate classification. A list of non-surgical cancer related treatments was collated (See  
4  
5 162 Appendix Table A3 for specific OPCS-4.7 procedure codes) and these costs were excluded in  
6  
7 163 the analysis. Peri-operative outcomes included mortality, conversion to open hysterectomy and  
8  
9 164 length of stay. The 90-day outcomes included the mortality, total and specific inpatient,  
10  
11 165 outpatient and emergency readmissions. Subgroup analyses were performed, firstly to assess  
12  
13 166 high cost (top 5% of costs at intervention by approach) and low-cost patients (lowest 50% of  
14  
15 167 costs at intervention by approach) in the cohort to assess what was driving high costs patients.  
16  
17 168 In addition, provider level analysis was conducted to assess hospital characteristics and costs  
18  
19 169 to further understand the impact of differing MIS rates and volume sizes.  
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23

### 24 170 ***Statistical Analyses***

25  
26  
27 171 A descriptive analysis of patient characteristics and data on costs and other health resource was  
28  
29 172 performed. The different approaches (LH, RH, OH, MIS) were then compared by using t-test  
30  
31 173 (for independent samples) and Wilcoxon rank-sum test (Mann-Whitney U test) for continuous  
32  
33 174 variable and for categorical variables by using the chi-squared tests. The average marginal  
34  
35 175 effect (AME)<sup>15</sup> was used to compare RH vs OH and RH vs LH on costing outcomes at  
36  
37 176 intervention, 30 days, 90 days and 365 days. This approach adjusted for patient age, ethnicity,  
38  
39 177 IMD rank, Charlson Comorbidity Index, year of procedure and whether a patient received  
40  
41 178 cancer treatment following the intervention (for further details see Appendix Table A3) by  
42  
43 179 fitting Generalised Linear Models (GLMS). The Modified Park Test & Pregibon's Link Test<sup>16</sup>  
44  
45 180 were used to ensure the most efficient model structure was used to model the costs. All  
46  
47 181 statistical analyses were performed using Stata 15®.  
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### 53 182 ***Patient and Public Involvement***

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55  
56 183 There was no patient or public involvement in the study planning or design.  
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## 185 RESULTS

186 A total of 35,304 procedures were performed, 18,604 (52.7%) LH, 1,801 (5.1%) RH, 14,291  
187 (40.5%) OH and 608 (1.7%) VH. The proportion of MIS cases increased significantly overtime  
188 each year from 46.6% in 2012/13 to 68.7% in 2016/17 ( $p<0.001$ ). This was primarily due to an  
189 increase in LH of 15.8% (44.7% to 60.5%), but there was also a 6.2% increase (2.0% to 8.2%)  
190 in the number of RH performed when comparing 2012/13 to 2016/17 as a proportion of all  
191 surgeries performed each year. Consequently, the number of OH cases decreased significantly  
192 overtime ( $p<0.001$ ) from 53.4% in 2012/13 to 31.3% in 2016/17 of cases in that year.

193 Table 1 presents the patient characteristics of the surgical approaches LH, RH and OH. Most  
194 cases were performed at high volume providers (>220 cases/year) with 72.4% for RH, 62.1%  
195 for LH and 60.9% for OH being undertaken at these providers (Table 1). As previously  
196 described, there was a significant difference in the social/racial characteristics of the patients  
197 undergoing MIS as compared to OH within this cohort of patients<sup>8</sup>. The characteristics of the  
198 RH population differed to patients undergoing LH; with a significantly higher percentage of  
199 RH patients having any co-morbidity from our defined list than LH (68.2% vs 64.0%,  $p<0.001$ ),  
200 more specifically the comorbidities of diabetes, hypertension and obesity all being higher  
201 proportion in RH cohort than LH cohort.

### 202 *Short-term costs by approach*

203 The short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach are  
204 presented in Table 2. LH was associated with the lowest mean cost at the intervention (£3069),  
205 30 (£3083), 90 (£3111) and 365 (£3169) days following the procedure. The mean cost for RH  
206 was significantly less than OH at all the time points ( $p<0.001$  for all). The average marginal  
207 effect (AME) for RH versus OH, controlling for patient characteristics, also showed a  
208 significant difference for RH over OH with the difference in cost increasing when comparing

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3 209 the unadjusted and AME value ( $p<0.001$  for all). Comparing RH and LH short-term costs, LH  
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5 210 costs were significantly lower for the unadjusted and AME differences ( $p<0.001$  for all). The  
6  
7 211 AME differences in cost between RH and LH were lower compared to the unadjusted  
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9 212 differences (e.g., AME difference of £108 vs. unadjusted difference of £260 at intervention).

### 213 ***High-Cost and Low-Cost Patient Comparison***

214 Assessing the top 5% highest cost (HC) patients of each approach (LH:  $n=336$ ; OH:  $n=593$ ,  
215 RH:  $n=27$ ) and comparing to the low-cost (LC) cohort, which was set at less than or equal to  
216 the median cost of the surgery (LH:  $n=12,913$ ; OH:  $n=9,021$ , RH:  $n=812$ ). The patients in the  
217 HC group were significantly older in all the routes of surgery (LH: 69.0 vs 65.7 years, OH:  
218 68.8 vs 65.1 years, RH: 67.5 vs 65.5 years:  $p<0.001$  for all). The HC cohort contained a higher  
219 percentage of patients from the lower socioeconomic groups (IMD Rank: 16637 vs 17287,  
220  $p<0.001$ ) and patients of non-white ethnicity (29.6% vs 19.2%,  $p<0.001$ ) as compared to the  
221 LC cohort. Patients in the HC cohort also had significantly greater number of co-morbidities  
222 compared to the LC cohort (CCI 1.82 vs 1.41 and any comorbidity 71.0% versus 63.9%  
223  $p<0.001$  for all). The length of hospital stay was significantly longer in the HC cases compared  
224 to the LC group (RH: 11.22 vs 1.84 days; LH: 11.42 vs 2.03 days; OH: 20.82 vs 3.71days;  
225  $p<0.001$  for all). Although the rate of complications was greater in the HC compared to the LC  
226 cohort (RH: 55.6% vs 14.0%; LH: 61.0% vs 16.2%; OH: 71.5% vs 19.1%;  $p<0.001$  for all),  
227 the rate was significantly lower with RH as compared to OH in both the HC and LC groups  
228 (HC: 55.6% vs 71.5%,  $p=0.075$ ; LC: 14.0% vs 19.1%,  $p<0.001$ ).

### 229 ***Patient Characteristics and Costs***

230 Patient characteristics, age and CCI, were associated with increasing costs for almost all routes  
231 of surgery at intervention, and 365 days following the procedure (Table 3). Assessing the age  
232 categories showed the costs at intervention were very similar for the <50 years, 50-59 years

233 and 60-69 years groups but gradually increased for each of the higher age groups. There was  
234 an increasing difference between the MIS and OH costs with rising age with the difference  
235 between MIS and OH for Age <50 being £258 increasing to a difference of £653 for Age >90  
236 years population. RH 365-day costs were significantly lower ( $p<0.01$ ) than OH in all age  
237 categories except 60-69 & 90> years. Comparing CCI showed that CCI group  $\geq 3$  was  
238 associated with the greatest difference in costs with the difference at 365 days between CCI  
239 group 1 and CCI group  $\geq 3$  being £130 for RH, £174 for LH and £759 for OH (Table 3).

240 Overtime patients who underwent RH had increasing levels of co-morbidities, when using the  
241 CCI score, and have in recent years had a higher average CCI than LH in 2015/16-2016/17  
242 (Figure 1). Comparing the cost of LH and RH against CCI score, identified that the costs closely  
243 reflected the patients' CCI. In 2012/13 when the RH population had a lower CCI then the costs  
244 were less, however, since 2014/15 the patient population undergoing RH higher CCI score and  
245 this was associated with a rise in the costs of RH above that of LH (Figure 1).

### 246 *Hospital Characteristics and Costs*

247 When exploring the association between provider volume, MIS rate and surgical costs there  
248 was an association with the MIS rate and cost, i.e. the greater the MIS rate the lower the cost  
249 (Figure 2). Many of the highest volume providers had higher average costs than providers with  
250 less volume, however the patient population undergoing surgery at the high volume providers  
251 were significantly older and had a higher CCI compared to the lower volume providers (Age:  
252 66.2 vs 65.6 years,  $p<0.001$ ; CCI: 1.47 vs 1.43,  $p<0.001$ ). The majority of the highest volume  
253 providers had MIS rates between 50% to 90% and the relationship held for high volume  
254 providers with average costs decreasing as MIS rates increased for the year 2016/17.

## 255 **DISCUSSION**

### 256 *Main findings*

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3 257 In this study, we have performed an in-depth analysis of real-world data and have identified  
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5 258 financial benefits for MIS as compared to OH for EC. We have demonstrated that LH has the  
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8 259 lowest mean cost at intervention and that costs increased with increasing patient age. In keeping  
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10 260 with other studies, we have also shown that OH, although attracting the lowest operative  
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12 261 consumable costs, had the greatest overall financial cost, even significantly higher than RH.  
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14 262 We have also identified that although the cost of RH is greater than LH, patients undergoing  
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16 263 RH have different characteristics compared to women having LH in recent years, and that cost  
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18 264 of surgery appears to be influenced by level of patients' co-morbidities and not the route of  
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20 265 surgery alone.  
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24 266 There will always be a proportion of cases that have to be performed OH due to contra-  
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26 267 indications/complications with MIS, which will inevitably attract higher costs due to their  
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28 268 complexity, but this can be reduced to low levels<sup>17</sup>. The significantly higher complication/re-  
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30 269 admission rate with OH have been reported previously<sup>8</sup> and in this study we have shown that  
31  
32 270 even in the HC groups, the complication rate was higher with OH (71.5%) as compared to RH  
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34 271 (55.6%) and LH (61.0%). A longer recovery time may impact on patient and employment  
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36 272 costs, with greater loss of earnings and longer return to work or contribution to society activities  
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38 273 as compared to MIS. Korsholm et al.<sup>18</sup>, reported no significant difference in return to the labour  
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40 274 market or use of sickness benefits in a study from Denmark however, in their study robotic  
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42 275 surgery was associated with greater cost than both laparoscopic and open hysterectomy, unlike  
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44 276 this UK analysis. Allowing for a number of OH cases, the disparity in MIS uptake across  
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46 277 England<sup>8</sup> does indicate that there is room for improvement in increasing the proportion of MIS  
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48 278 cases and thereby benefitting both the patient and the healthcare economy.  
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55 279 The primary argument used against the widespread use of RH, rather than LH, for EC is an  
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57 280 economic one<sup>6,19</sup>, since the clinical outcomes are reported to be comparable although, there is  
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59 281 a lack of randomised control trial data, particular in patients with a high BMI<sup>20</sup>. The HES data

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3 282 does confirm a cost advantage for LH over RH however, the two patient populations are not  
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5 283 directly comparable since there is a significant difference in the CCIs between the groups.  
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7 284 During 2012/13, when RH was only performed in a few selected centres, the majority of UK  
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9 285 robotic surgeons would still have been within the learning phase, and therefore likely to select  
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11 286 patients with less co-morbidities for RH. We have shown that during this time period the cost  
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13 287 of RH was less than LH. Increasing robotics experience appears to have led to the positive  
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15 288 selection of co-morbid patients, especially obesity, for RH, and this is associated with rising  
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17 289 costs. Class III obesity and a rising number of patient co-morbidities are reported to attract  
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19 290 increased inpatient care costs due to increased medical rather than surgical complications  
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21 291 associated with undergoing surgery<sup>21,22</sup>. The selection of patients with a high-BMI for RH is  
22  
23 292 not unexpected given the reported ergonomic benefits for surgeons as compared to straight-  
24  
25 293 stick laparoscopy<sup>23</sup>, with less movements and muscle activity required to perform tasks<sup>24</sup>. RH  
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27 294 is not without issues due to the fixed console position<sup>25</sup>, however more extreme muscle  
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29 295 movements are required for laparoscopic procedures increase with rising BMI<sup>24</sup>, which is not  
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31 296 reported with robotics. The cost to the healthcare service of work-related musculoskeletal  
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33 297 symptoms in surgeons is of growing concern<sup>26</sup> and not considered in economic analyses such  
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35 298 as this study, however it is an additional cost that needs to be considered when calculating  
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37 299 service delivery costs.

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40 300 What is clear from the data is that OH is the most costly route of surgery, a finding reported in  
41  
42 301 other healthcare settings<sup>27</sup>, not only in financial terms but more importantly for patient  
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44 302 complications and post-operative mortality<sup>8</sup>. The key focus therefore, rather than being  
45  
46 303 between LH or RH, should instead be on reducing the OH rate to a minimum. Although there  
47  
48 304 are only a few absolute contra-indications for OH, the number of cases that are performed  
49  
50 305 through open surgery is still high in some institutions and there has been much discussion how  
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52 306 this could be reduced through greater surgical training<sup>28</sup> or centralisation of cases to hospitals  
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3 307 and surgeons with high MIS rates<sup>29</sup>. A reduction in OH can also be achieved through reducing  
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5 308 the number of conversions from LH/RH to a minimum. A meta-analysis of observational  
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7 309 studies did show that the conversion rate of LH increased with BMI >40kg/m<sup>2</sup> more than for  
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9 310 RH, 6.5% (95% CI 4.3-9.9) versus 5.5% (95% CI 3.3-9.1), as compared to >30kg/m<sup>2</sup>, 7.0%  
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11 311 (95% CI 3.2-14.5) versus 3.8% (95% CI 1.4-9.9) respectively<sup>20</sup>. One reason for this may be the  
12  
13 312 lower intra-abdominal insufflation pressure used with RH, typically 8mmHg, which has been  
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15 313 shown to be associated with lower post-operative pain and shorter hospital stay as compared  
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17 314 to a pressure 15mmHg<sup>30</sup>. Inability to tolerate Trendelenburg position was also reported to be  
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19 315 the indication for 31% of LH conversions but only 6% of RH conversions<sup>20</sup>. This therefore  
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21 316 raises the possibility as to whether cases should be selected for RH where there is high risk of  
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23 317 conversion due to Class III obesity or inability tolerate the pneumoperitoneum. Further research  
24  
25 318 is needed to compare the clinical outcomes and costs of LH and RH in matched populations,  
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27 319 for example BMI >40kg/m<sup>2</sup> or previous abdominal surgery, to investigate whether differences  
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29 320 reported in retrospective case series are confirmed. Such trials would determine whether certain  
30  
31 321 patient characteristics could be used to personalise the route of surgery in order to maximise  
32  
33 322 the potential benefit from MIS and reduce the rate of OH. Prospective randomised controlled  
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35 323 trials (RCT) are the gold standard study design however can be challenging to perform and  
36  
37 324 may be subject to many biases, including patient selection, if a surgeon has a greater preference  
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39 325 for one surgical modality over another. Also, RCTs can take many years to complete accrual,  
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41 326 for example LACC<sup>31</sup>, by which time the current robotic/laparoscopic platforms may be  
42  
43 327 obsolete. Instead, the use of real-world data in a propensity score matching study may enable  
44  
45 328 matching of key patient characteristics to give results in a more timely manner<sup>32</sup>.

### 329 ***Strengths and limitations***

330 The key strength of the study is in the number of patients in which can be analysed by using  
331 the HES database. This gives strength to the study's findings as it is representative of all



1  
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3 332 procedures via the NHS in England. Due to RH being a newer surgery approach the number of  
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5 333 patients is much lower compared to the other surgery approaches. In addition, we must consider  
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8 334 the impact of a learning curve of RH and that in the earlier years it may not been used to full  
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10 335 efficiency. As we had a number of years of the HES database we could analyse any potential  
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12 336 trends across surgical approaches and the year.

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15 337 As we have previously described<sup>8</sup>, HES data does have limitations, primarily it only covers  
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17 338 NHS-funded care, the reliability of coding and lacks oncological details of stage/histology.  
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20 339 There will be a proportion of patients with advanced disease that require open surgery due to  
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22 340 requiring a more extensive cytoreductive procedure and HES data is not able to differentiate  
23  
24 341 these cases from early stage disease that is being treated through open surgery. The analysis  
25  
26 342 comparing LH and RH should however not be impacted by stage of disease. In addition, there  
27  
28 343 are limitations with the HES data with the recording of magnitude of patient co-morbidities, in  
29  
30 344 particular obesity since a numerical value for BMI is not included and therefore the obesity  
31  
32 345 classification could be applied to any patient with a BMI >30kg/m<sup>2</sup>.

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35 346 The capital and maintenance costs of RH have also not been included since these costs vary  
36  
37 347 dramatically across different healthcare settings and there would be a need to also included  
38  
39 348 similar costs for laparoscopic and open surgery. In addition, the robotic surgery equipment is  
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41 349 often utilised by a wide group of specialities in a hospital setting and it would be infeasible to  
42  
43 350 apply capital and maintenance costs to one surgery modality<sup>15</sup>.

### 44 45 46 47 48 351 ***Interpretation***

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51 352 In conclusion, LH was associated with the lowest and OH the greatest mean cost per procedure.  
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53 353 Patient factors have an impact on the cost of MIS procedures and further research is needed to  
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55 354 compare the costs in matched populations of women undergoing LH and RH, since there  
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57 355 appears to be selection bias in the choice of procedure being performed.  
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1  
2  
3 356 **Ethical approval:** The HES database is managed by the NHS Digital and is available for  
4  
5 357 research without ethical approval.  
6

7 358  
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9 359 All the authors consent to publication  
10

11 360  
12  
13 361 **Data availability:** Data analysed in this study is available through Hospital Episode Statistics  
14  
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16 362 (HES)  
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18  
19 363 **Conflicts of Interest:** EM and TI perform Da’Vinci robotic gynaecological surgery (Intuitive  
20  
21 364 Surgical) and are members of the British and Irish Association of Robotic Surgeons (BIARGS),  
22  
23 365 which is supported by Intuitive Surgical and other robotics/laparoscopic companies to hold  
24  
25 366 education/training events. EM has been awarded research grants from Intuitive Surgical and  
26  
27 367 Hope Against Cancer for unrelated studies, serves on advisory boards for Inivata and  
28  
29 368 GlaxoSmithKline and has received speaker fees from GlaxoSmithKline. TI has done two days  
30  
31 369 paid consultancy work for Medtronic. GM and AM from HCD Economics were funded by  
32  
33 370 Intuitive Surgical. None of the clinicians (EM, PS, TI) received funding from Intuitive Surgical  
34  
35 371 for this study. Intuitive Surgical did not have any involvement with the study design, data  
36  
37 372 analysis and writing of the manuscript. The authors declare no other potential conflict of  
38  
39 373 interest.  
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48 375 **Contributors:** EM, TI, GM and AM contributed to the conceptualisation and study design.  
49  
50 376 Data analysis and interpretation was performed by EM, TI, GM, AM and PS. Figures and tables  
51  
52 377 creation was performed by EM, GM and AM. All authors were involved in the writing or  
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54 378 review of the manuscript and approved the final version.  
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6  
7 381 & Social Care Information Centre 2018.  
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10  
11 382 **Figure 1: Intervention Cost & CCI Over Time**

12 383 The average cost and CCI of RH & LH over time.

13  
14 384 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic  
15 385 hysterectomy, NHS = National Health Service)

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17 386 **Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17**

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19 387 The association between provider volume, MIS rate and surgical cost at intervention. Provider  
20 388 volume is represented by the size of the bubble with a larger bubble representing a higher  
21 389 provider volume.  
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507 **Table 1. Clinical and Demographic Characteristics by the cohorts of hysterectomy approach**

Characteristics	Unadjusted Results							
	Laparoscopic Hysterectomy (N=18604)		Robotic Hysterectomy (N=1801)		MIS Hysterectomy (N=20405)		Open Hysterectomy (N=14291)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<b>NHS Year of surgery</b>								
2011/12*	1,108	6%	19	1%	1,127	6%	1,671	12%
2012/13	2,367	13%	104	6%	2,471	12%	2,829	20%
2013/14	2,824	15%	147	8%	2,971	15%	2,614	18%
2014/15	3,134	17%	253	14%	3,387	17%	2,361	17%
2015/16	3,118	17%	382	21%	3,500	17%	1,948	14%
2016/17	3,577	19%	483	27%	4,060	20%	1,852	13%
2017/18*	2,476	13%	413	23%	2,889	14%	1,016	7%
<b>Age, years</b>								
<50	1,033	6%	120	7%	1,153	6%	1,082	8%
50-59	3,937	21%	380	21%	4,317	21%	3,098	22%
60-69	6,522	35%	589	33%	7,111	35%	4,672	33%
70-79	5,160	28%	533	30%	5,693	28%	3,779	26%
80-89	1,846	10%	174	10%	2,020	10%	1,540	11%
90>	106	1%	5	0%	111	1%	120	1%
<b>Ethnicity</b>								
White	15,033	81%	1,420	79%	16,453	81%	11,117	78%
Asian	583	3%	66	4%	649	3%	499	3%
Black	231	1%	20	1%	251	1%	365	3%
Other	2,757	15%	295	16%	3,052	15%	2,310	16%
<b>Socio-Economic Group (IMD)</b>								

High	4,506	25%	643	37%	5,149	25%	3,291	23%
Intermediate	4,612	25%	403	23%	5,015	25%	3,387	24%
Low	4,548	25%	376	21%	4,924	24%	3,489	24%
Very Low	4,435	25%	333	19%	4,768	23%	3,703	26%
<b>Charlson Comorbidity Group</b>								
0	22	0%	1	0%	23	0%	13	0%
1	12,432	67%	1,159	64%	13,591	67%	8,405	59%
2	4,915	26%	514	29%	5,429	27%	4,535	32%
>=3	1,235	7%	127	7%	1,362	7%	1,338	9%
<b>Region</b>								
Greater London	2,529	14%	319	18%	2,848	14%	2,184	15%
Yorkshire	1,501	8%	270	15%	1,771	9%	1,220	9%
West Midlands	1,747	9%	154	9%	1,901	9%	1,672	12%
South West	2,676	14%	75	4%	2,751	13%	1,348	9%
South East	1,746	9%	339	19%	2,085	10%	1,451	10%
North West	2,628	14%	281	16%	2,909	14%	2,550	18%
North East	1,264	7%	138	8%	1,402	7%	432	3%
Home Counties	1,095	6%	31	2%	1,126	6%	912	6%
East Midlands	1,485	8%	165	9%	1,650	8%	1,003	7%
East	1,922	10%	4	0%	1,926	9%	1,497	10%
<i>Missing</i>	11	0%	25	1%	36	0%	22	0%
<b>Provider Volume</b>								
High	11,423	62%	1,302	72%	12,725	62%	8,703	61%
Intermediate	6,653	36%	487	27%	7,140	35%	5,102	36%
Low	279	2%	9	1%	288	1%	191	1%
Very Low	36	0%	0	0%	36	0%	58	0%
<i>Missing</i>	213	1%	3	0%	216	1%	237	2%

\*NHS Year 2011/12 & 2017/18 not full year

510 **Table 2. Short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach**

	Mean Cost in £ (SD)			Difference RH vs OH				Difference RH vs LH			
	RH (N =1353)	OH (N=12379)	LH (N=15666)	Unadjusted Difference (£)	P Value	AME (£) *	P Value	Unadjusted Difference (£)	P Value	AME (£) *	P Value
<b>At Intervention</b>	3329 (713)	3349 (1318)	3069 (676)	-20	<0.001	-197	<0.001	260	<0.001	108	<0.001
<b>At 30 days</b>	3334 (722)	3379 (1395)	3083 (721)	-45	<0.001	-220	<0.001	251	<0.001	98	<0.001
<b>At 90 days</b>	3357 (761)	3424 (1468)	3111 (826)	-67	<0.001	-241	<0.001	246	<0.001	89	<0.001
<b>At 365 days</b>	3417 (906)	3533 (1687)	3169 (984)	-116	<0.001	-273	<0.001	248	<0.001	94	<0.001

511 \*AME adjusted for Year, Age, Socioeconomic Status (IMD Rank), Charlson Comorbidity, Ethnicity, Cancer Tx

512 Notes:

513 RH vs OH: We see that the average marginal effect is greater than the actual difference between RH and OH when we control for covariates

514 RH vs LH: We see the average marginal effect is less than the actual difference between RH and LH when we control for covariates

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6/bmjopen-2020-045888 on 13 May 2021. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



522 **Table 3. Mean Cost at intervention and 365 days by CCI/Age for each approach**

	LH			RH			MIS			OH	
	N	Mean (SD)	P-Value*	N	Mean (SD)	P-Value*	N	Mean (SD)	P-Value*	N	Mean (SD)
<b>Age Groups (Costs at Intervention)</b>											
<50	860	£3032 (616)	<0.001	90	£3284 (942)	0.783	950	£3056 (657)	<0.001	921	£3314 (1325)
50-59	3336	£3025 (558)	<0.001	293	£3258 (593)	0.967	3629	£3044 (565)	<0.001	2687	£3259 (1033)
60-69	5522	£3053 (657)	<0.001	436	£3357 (819)	0.089	5958	£3075 (675)	<0.001	4077	£3283 (1173)
70-79	4328	£3101 (732)	<0.001	398	£3343 (600)	0.052	4726	£3121 (725)	<0.001	3255	£3419 (1406)
80-89	1533	£3149 (777)	<0.001	134	£3385 (716)	0.041	1667	£3168 (774)	<0.001	1338	£3546 (1782)
90>	87	£3215 (1311)	0.023	<10	£3454 (687)	0.461	89	£3220 (1298)	0.023	101	£3855 (2425)
<b>CCI Groups (Costs at Intervention)</b>											
0	21	£3060 (292)	0.156	<10	£3939 (0)	-	22	£3100 (341)	0.078	12	£2968 (0)
1	10526	£3038 (616)	<0.001	887	£3319 (763)	0.010	11413	£3060 (633)	<0.001	7369	£3247 (994)
2	4126	£3126 (777)	<0.001	377	£3337 (607)	0.051	4503	£3143 (767)	<0.001	3875	£3412 (1375)
>=3	993	£3166 (806)	<0.001	88	£3391 (614)	<0.001	1081	£3184 (794)	<0.001	1123	£3808 (2421)
<b>Age Groups (Costs at 365 days)</b>											
<50	860	£3136 (900)	<0.001	90	£3287 (945)	0.005	950	£3150 (905)	<0.001	921	£3615 (1821)
50-59	3336	£3111 (903)	<0.001	293	£3274 (612)	0.005	3629	£3125 (884)	<0.001	2687	£3399 (1373)
60-69	5522	£3144 (922)	<0.001	436	£3476 (1091)	0.638	5958	£3169 (940)	<0.001	4077	£3449 (1503)
70-79	4328	£3219 (1103)	<0.001	398	£3468 (836)	0.008	4726	£3240 (1086)	<0.001	3255	£3607 (1806)
80-89	1533	£3256 (1017)	<0.001	134	£3477 (925)	0.003	1667	£3274 (1011)	<0.001	1338	£3776 (2169)
90>	87	£3252 (1350)	0.003	<10	£3454 (687)	0.200	89	£3257 (1337)	0.003	101	£4175 (2774)
<b>CCI Groups (Costs at 365 days)</b>											
0	21	£3074 (294)	0.106	<10	£3939 (0)	-	22	£3114 (341)	0.054	12	£2968 (0)
1	10526	£3126 (891)	<0.001	887	£3358 (827)	0.323	11413	£3144 (888)	<0.001	7369	£3390 (1368)
2	4126	£3249 (1160)	<0.001	377	£3538 (1088)	0.148	4503	£3273 (1157)	<0.001	3875	£3629 (1745)
>=3	993	£3299 (1097)	<0.001	88	£3488 (747)	<0.001	1081	£3315 (1073)	<0.001	1123	£4148 (2832)

\*Significance test were carried out against the OH category within each age/CCI group for the approaches LH, RH and MIS

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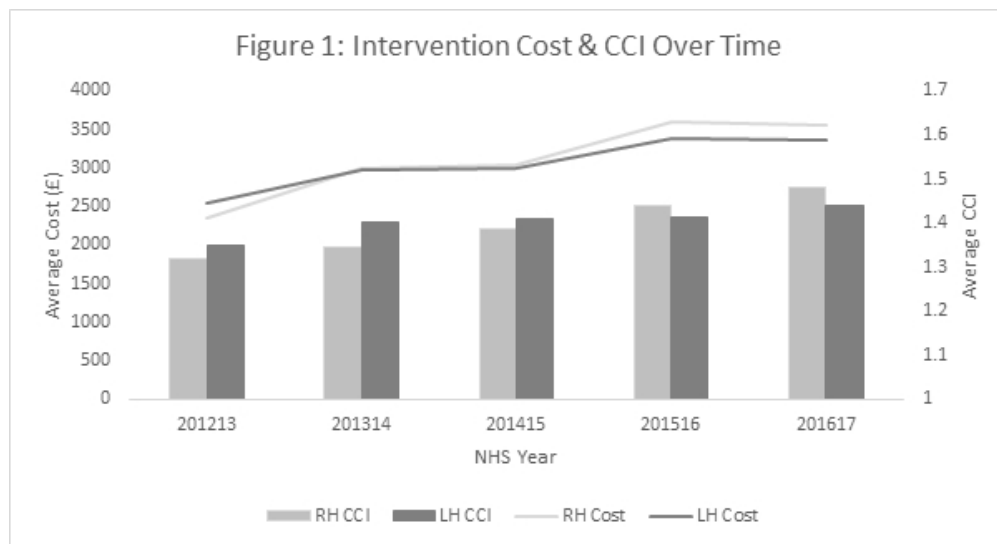


Figure 1: Intervention Cost & CCI Over Time  
 The average cost and CCI of RH & LH over time.  
 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic hysterectomy, NHS = National Health Service)

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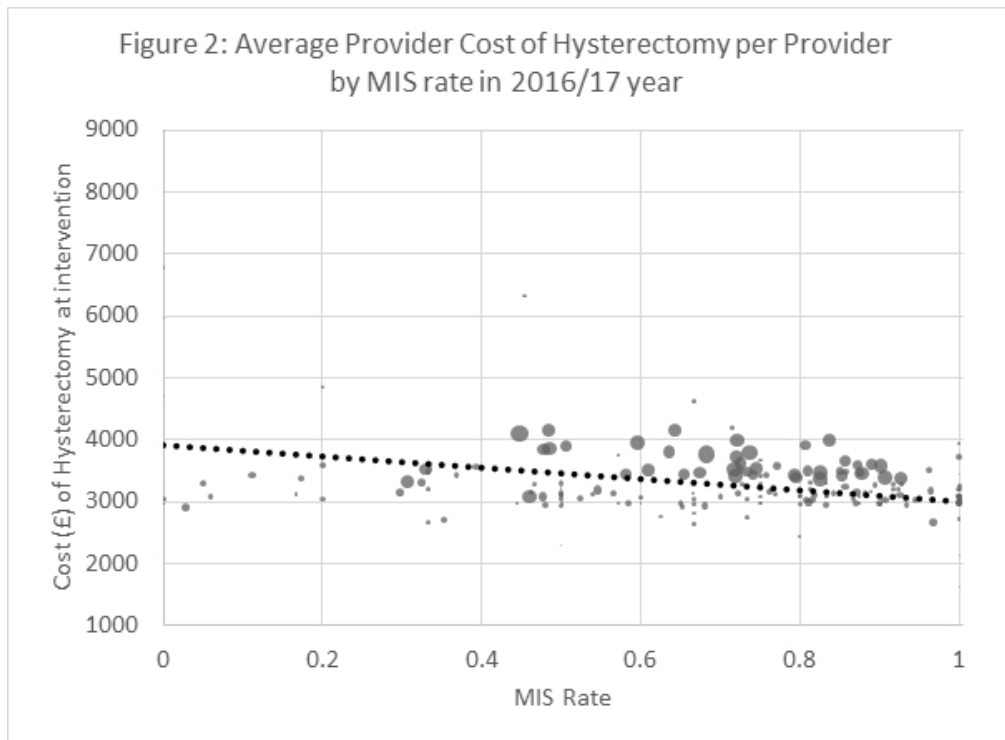


Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17  
 The association between provider volume, MIS rate and surgical cost at intervention. Provider volume is represented by the size of the bubble with a larger bubble representing a higher provider volume.

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## Appendix Tables:

Table A1- Cohort Selection ICD-10 & OPCS-4.7 Codes

Table A1: Cohort Selection

Category	ICD-10 / OPCS-4.7
<b>Hysterectomies</b>	Procedures with: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9
<b>Endometrial/uterine carcinoma or endometrial carcinoma in situ</b>	Patients must have as primary diagnosis: C540, C541, C542, C543, C548, C549, C55X, D070
<b>Laparoscopic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9
<b>Robotic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.3
<b>Open hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Vaginal hysterectomy</b>	Any procedures with one of: Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Minimally Invasive Surgery</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9, Y75.3

Table A2 – Other complications OPCS-4.7 codes assessed

Table A2: Complication classification<sup>a</sup>

Category	ICD-10 / OPCS-4.7
<b>Gastrointestinal complications</b>	A090 I898 K228 K250 K252 K254 K256 K260 K261 K262 K264 K265 K266 K270 K272 K274 K276 K280 K282 K284 K286 K290 K450 K560 K565 K566 K567 K625 K631 K638 K660 K720 K729 K85 K913 K918 K919 K92 S360 K61 N824
<b>Wounds</b>	D649 K603 K604 K605 K632 K829 K832 L89 T813 T815 T343 T453 T793
<b>Infections</b>	A40 A41 A49 B95 B96 K630 K65 L03 L04 N10 N12 N151 N159 N300 N309 N390 R788 T793 T802 T814 T816 T827 T836 T857
<b>Uteric Injury Complication</b>	N133 N139 N17 N19 N280 N312 N990 N991 N998 N999 R32 R33 S360 N12 N151 N159 N300 N309 N390 N360 S371 N131 N821
<b>Haemorrhage</b>	T810 S35 D65
<b>Cardiovascular disorders</b>	I21 I46 I48 I49 I50 I74 I80 I81 I82 I950 I952 I959 I978 I979 R57 T801 T811 T817 T827
<b>Pulmonary complications</b>	J80 J81 J90 J91 J93 J955 J958 J959 J960 J969 J981 R060 R09 I26 J100 J110 J12 J13 J14 J15 J16 J17 J18 J690 J85 J86
<b>Neurological disorders</b>	F05 F13 F15 F19 G45 G46 G569 G81 G82 G83 G931 G936 G970 G971 G978 G979 I63 I65
<b>Other</b>	T882 T790 T800 E15 E272 E86 E87 R798 T812 T818 T888 T792

<sup>a</sup> Adapted from Ma C, et al. Postoperative complications following colectomy for ulcerative colitis: A validation study. BMC Gastroenterol 2012; 12:39.

Table A3: Cancer Treatment OPCS 4.7 Codes excluded for cost analysis

Category	Specific Code	Sub Category
Chemotherapy	X70.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 1
	X70.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 2
	X70.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 3
	X70.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 4
	X70.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 5
	X70.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X70.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X71.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 6
	X71.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 7
	X71.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 8
	X71.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 9
	X71.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 10
	X71.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X71.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X72.1	Delivery of complex chemotherapy for neoplasm including prolonged infusional treatment at first attendance
	X72.2	Delivery of complex parenteral chemotherapy for neoplasm at first attendance
	X72.3	Delivery of simple parenteral chemotherapy for neoplasm at first attendance
	X72.4	Delivery of subsequent element of cycle of chemotherapy for neoplasm
	X72.8	Other specified delivery of chemotherapy for neoplasm
	X72.9	Unspecified delivery of chemotherapy for neoplasm
	X73.1	Delivery of exclusively oral chemotherapy for neoplasm
	X73.8	Other specified delivery of oral chemotherapy for neoplasm
	X73.9	Unspecified delivery of oral chemotherapy for neoplasm
	X74.1	Cancer hormonal treatment drugs Band 1
	X74.2	Cancer supportive drugs Band 1
	X74.8	Other specified other chemotherapy drugs
	X74.9	Unspecified other chemotherapy drugs
	Radiotherapy	X65.1
X65.2		Delivery of a fraction of intracavitary radiotherapy
X65.3		Delivery of a fraction of interstitial radiotherapy
X65.4		Delivery of a fraction of external beam radiotherapy NEC
X65.5		Oral delivery of radiotherapy for thyroid ablation
X65.6		Delivery of a fraction of intraluminal brachytherapy
X65.7		Delivery of radionuclide therapy NEC
X65.8		Other specified radiotherapy delivery
X65.9		Unspecified radiotherapy delivery
X67.1		Preparation for intensity modulated radiation therapy
X67.2		Preparation for total body irradiation
X67.3		Preparation for hemi body irradiation
X67.4		Preparation for simple radiotherapy with imaging and dosimetry
X67.5		Preparation for simple radiotherapy with imaging and simple calculation
X67.6		Preparation for superficial radiotherapy with simple calculation
X67.7		Preparation for complex conformal radiotherapy
X67.8	Other specified preparation for external beam radiotherapy	

	X67.9	Unspecified preparation for external beam radiotherapy
	Y92.1	Technical support for preparation for radiotherapy
	Y92.2	Other specified support for preparation for radiotherapy
	Y92.3	Unspecified support for preparation for radiotherapy
Brachytherapy	X68.1	Preparation for intraluminal brachytherapy
	X68.2	Preparation for intracavitary brachytherapy
	X68.3	Preparation for interstitial brachytherapy
	X68.8	Other specified preparation for brachytherapy
	X68.9	Unspecified preparation for brachytherapy
	Y35.4	Introduction of radioactive substance into organ for brachytherapy NOC
	Y36.4	Introduction of non-removable radioactive substance into organ for brachytherapy NOC
	Y89.1	High dose rate brachytherapy treatment
	Y89.2	Pulsed dose rate brachytherapy treatment
	Y89.8	Other specified brachytherapy
	Y89.9	Unspecified brachytherapy

**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies**

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			



Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9 9 NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9 (Table 1) 9 (Table 1) 9
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11 9-11 NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12-14
<b>Limitations</b>			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-15
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Economic evaluation of different routes of surgery for the management of endometrial cancer: A retrospective cohort study.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-045888.R2
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Date Submitted by the Author:	22-Apr-2021
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Secondary Subject Heading:	Obstetrics and gynaecology, Oncology
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3 **1 Economic evaluation of different routes of surgery for the management of endometrial**  
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5 **2 cancer: A retrospective cohort study.**  
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20 **Word count: 3575**  
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3 **23 ABSTRACT**  
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6 **24 Objectives:** The benefits of minimally invasive surgery (MIS) for endometrial carcinoma (EC)  
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9 **25** are well established although the financial impact of robotic-assisted hysterectomy (RH)  
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11 **26** compared to laparoscopic hysterectomy (LH) is disputed.

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14 **27 Design:** Retrospective cohort study.

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17 **28 Setting:** English NHS hospitals 2011-2017/8.

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20 **29 Participants:** 35,304 women having a hysterectomy for EC identified from Hospital Episode  
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22 **30** Statistics (HES).

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25 **31 Primary and secondary outcome measures:** The primary outcome was the association  
26  
27 **32** between route of surgery on cost at intervention, 30, 90 and 365 days for women undergoing  
28  
29 **33** an open (OH) or MIS (LH/RH) for EC in England. The average marginal effect (AME) was  
30  
31 **34** calculated to compare RH vs OH/RH vs LH which adjusted for any differences in the  
32  
33 **35** characteristics of the surgical approaches. Secondary outcomes were to analyse costing data  
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35 **36** for each surgical approach by age, Charlson Comorbidity Index (CCI) and hospital MIS rate  
36  
37 **37** classification.

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40 **38 Results:** A total of 35,304 procedures were performed, 20,405 (57.8%) were MIS (LH 18,604  
41  
42 **39** and RH 1,801), 14,291 (40.5%) OH. Mean cost for LH was significantly less than RH, whereas  
43  
44 **40** RH was significantly less than OH at intervention, 30, 90 and 365 days ( $p < 0.001$ ). Overtime  
45  
46 **41** patients who underwent RH had increasing CCI scores and by the 2015/16 year had a higher  
47  
48 **42** average CCI than LH. Comparing the cost of LH and RH against CCI score identified that the  
49  
50 **43** costs closely reflected the patients' CCI. Increasing disparity was also seen between the MIS  
51  
52 **44** and OH costs with rising age. When exploring the association between provider volume, MIS  
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54 **45** rate and surgical costs there was an association with the higher the MIS rate the lower the  
55  
56 **46** average cost.  
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3 47 **Conclusions:** Further research is needed to investigate costs in matched patient cohorts to  
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5 48 determine optimum surgical modality in different populations.  
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15  
16 52 applicable. None of the clinicians involved in this study received funding from Intuitive  
17  
18 53 Surgical. Intuitive Surgical did not have any involvement with the study design, data analysis  
19  
20 54 or writing of the manuscript.  
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23

24 55 **Key words:** Endometrial cancer; minimally invasive surgery; laparoscopic hysterectomy; open  
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26 56 hysterectomy; robotic-assisted hysterectomy; patient stratification; healthcare economy  
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32 58 **Tweetable abstract:** Analysis of financial cost of laparoscopic, robotic and open hysterectomy  
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34 59 for the treatment of endometrial cancer in England.  
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3 68 ***Strengths and limitations***  
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- 6 69 • The findings from the study are based on a population-based database which is a key  
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8 70 strength as it is representative of all procedures via the NHS in England.  
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11 71 • The reliability of the coding might have changed over time although there was no  
12  
13 72 evidence of changes in treatment coding or significant changes in the underlying study  
14  
15 73 population.  
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17  
18 74 • HES database reliably captures extensive amount of demographic, diagnosis and  
19  
20 75 procedure outcomes however there is a lack of cancer stage information therefore it is  
21  
22 76 not possible to split out the cost outcomes into more specific groups of patients.  
23  
24  
25 77 • The capital and maintenance costs of RH have also not been included since these costs  
26  
27 78 vary dramatically across different healthcare settings and often utilised by a wide group  
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29 79 of specialities in a hospital setting.  
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31  
32 80 • As the analysis was undertaken over a number of years of the HES database, we were  
33  
34 81 able to accurately follow hospital activity for at least a year after intervention.  
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## 90 INTRODUCTION

91 The introduction of minimally invasive surgery (MIS) for endometrial cancer (EC) has had a  
92 dramatic impact on patients' surgical outcomes with reduced morbidity, hospital stay and  
93 improved short-term quality of life<sup>1</sup>. Translating these patient benefits into cost benefits to the  
94 healthcare economy has been challenging because although MIS requires significantly less bed  
95 days than open surgery, it does require more costly consumable equipment, for example single-  
96 use vessel sealing devices. This has been demonstrated in several studies including the multi-  
97 centre randomised LACE trial where the surgery costs were greater for laparoscopic  
98 hysterectomy (LH) compared to open hysterectomy (OH), but the overall costs of treatment  
99 were lower<sup>2</sup>.

100 MIS is the preferred surgical route for EC<sup>3</sup>. RH is accepted as an alternative to LH, supported  
101 by evidence from a randomised controlled trial<sup>4</sup> and RH has been shown to have a lower  
102 conversion rate to laparotomy and shorter operating time<sup>5-7</sup>. Wide spread adoption of RH is  
103 limited in England, although the number of EC cases having RH is increasing year on year<sup>8</sup>. In  
104 light of the capital and consumable costs of RH, as compared to OH or LH, the use of RH in  
105 EC is therefore being called into question<sup>6</sup>. Reports from institutions with well-established  
106 robotic programmes however have contested this view with no significant difference<sup>9</sup>, or cost  
107 improvements reported as compared to LH<sup>10</sup>. What is clear is that focusing solely on in-hospital  
108 costs does not give the full picture of the economic costs of a surgical procedure, since many  
109 costs are accrued following discharge or attributed to the economy as a whole as a result of  
110 delayed return to employment.

111 We therefore investigated the HES data for England in order to look at the financial impact of  
112 RH as compared to LH and OH. We also investigated the patient characteristics that contributed



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3 113 to cost and examined the top 5% of procedures to identify factors that may have contributed to  
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5 114 the costs.  
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## 8 115 **METHODS**

### 10 116 *Data Source and cohort selection*

11 117 Data was sourced from the Hospital Episode Statistics (HES) database from 2011-2017/8<sup>11</sup>.  
12  
13  
14 118 HES database captures demographic, diagnosis and procedure outcomes data however does  
15  
16 119 not include cancer stage or histology information. No ethical approval was required for this  
17  
18 120 study. Patients or the public were not involved in the design, or conduct, or reporting of our  
19  
20 121 research. The inclusion criteria for patients was a diagnosis of endometrial cancer (EC) or  
21  
22 122 endometrial cancer in situ/complex atypical hyperplasia (ECIS) undergoing a hysterectomy  
23  
24 123 between October 2011 to December 2017. The surgical approach was classified by intention-  
25  
26 124 to-treat as open hysterectomy (OH), vaginal hysterectomy (VH), laparoscopic hysterectomy  
27  
28 125 (LH), robotic hysterectomy (RH) and minimally invasive surgery (MIS) which was the  
29  
30 126 combination of LH and RH. Due to the low numbers the VH cases were not included in any of  
31  
32 127 the subsequent analyses. The cohort selection for the study has been described in more detail  
33  
34 128 previously<sup>8</sup> and the list of specific diagnosis (ICD-10) and procedure (OPCS-4.7) codes can be  
35  
36 129 found in the Appendix Table A1.  
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### 45 130 *Patient Characteristics*

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48 131 Demographic data was captured in the hospital admission data for each patient and included  
49  
50 132 age, ethnicity, postcode, comorbidities. Patient age was divided by 10-year intervals from the  
51  
52 133 age of 50 into six groups. Ethnicity was classified into Asian, Black, Other and White ethnicity.  
53  
54 134 Based on postcode of residence, each patient who received EC surgery was mapped to the  
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56 135 English Index of Multiple Deprivation rank. The IMD indicates the socioeconomic deprivation  
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59 136 of patients which combines seven indicators (income, employment, health deprivation and  
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3 137 disability, education, skills and training, barriers to housing and services, crime, and living  
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5 138 environment), into a single deprivation index where a higher rank indicated a less deprived  
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8 139 group and a lower rank indicated a more deprived group<sup>12</sup>. The Index of Multiple Deprivation  
9  
10 140 (IMD) was split into statistical quartiles and indicated whether the sociodemographic status  
11  
12 141 was high (>25083), intermediate (17475-25083), low (9618-17474) or very low (<9618) for  
13  
14 142 each patient. Comorbidities were examined 12 months prior to intervention using the Charlson  
15  
16 143 Comorbidity Index (CCI)<sup>13</sup>, an additional list of other co-morbidities were also assessed using  
17  
18 144 specific ICD-10 codes (Appendix Table A2).

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22 145 Hospital characteristics were assessed by region (East, East Midlands, Greater London, Home  
23  
24 146 Counties, North East, North West, South East, South West, West Midlands, Yorkshire) and  
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26  
27 147 volume, which was based on the annual mean of hysterectomies performed for EC/ECIS  
28  
29 148 grouped by statistical quartiles (High (>220), Intermediate (71-220), Low (70-21) and Very  
30  
31 149 Low (0-20)). MIS rates of hospitals for EC/ECIS hysterectomy procedures were classified into  
32  
33 150 four groups based on percentage of hysterectomies performed by MIS approach (High (76-  
34  
35 151 100%), Intermediate (51-75%), Low (26-50%) and Very Low (0-25%)).

### 38 39 152 *Outcomes*

40  
41  
42 153 For each patient episode, in the HES database, a cost is assigned based on the health resource  
43  
44 154 group (HRG) which is diagnosis/procedure-based grouping and the length of stay. These costs  
45  
46 155 are based on reference costs provided by each hospitals and are estimated based upon recorded  
47  
48 156 inpatient, outpatient, and A&E episode activity in the HES database using NHS Payment by  
49  
50 157 Results Health Resource Group (HRG) tariffs<sup>14</sup>. Costs at intervention and short-term costs were  
51  
52 158 calculated based upon the reported hospital admission costs over the time period of 30-, 90-  
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54 159 and 365-days following intervention, these were all summarised by procedure approach.  
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57 160 Further to this, the cost of each approach was assessed by the subgroups of age, CCI groups

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3 161 and MIS rate classification. A list of non-surgical cancer related treatments was collated (See  
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5 162 Appendix Table A3 for specific OPCS-4.7 procedure codes) and these costs were excluded in  
6  
7 163 the analysis. Peri-operative outcomes included mortality, conversion to open hysterectomy and  
8  
9 164 length of stay. The 90-day outcomes included the mortality, total and specific inpatient,  
10  
11 165 outpatient and emergency readmissions. Subgroup analyses were performed, firstly to assess  
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13 166 high cost (top 5% of costs at intervention by approach) and low-cost patients (lowest 50% of  
14  
15 167 costs at intervention by approach) in the cohort to assess what was driving high costs patients.  
16  
17 168 In addition, provider level analysis was conducted to assess hospital characteristics and costs  
18  
19 169 to further understand the impact of differing MIS rates and volume sizes.  
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### 24 170 ***Statistical Analyses***

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26  
27 171 A descriptive analysis of patient characteristics and data on costs and other health resource was  
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29 172 performed. The different approaches (LH, RH, OH, MIS) were then compared by using t-test  
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31 173 (for independent samples) and Wilcoxon rank-sum test (Mann-Whitney U test) for continuous  
32  
33 174 variable and for categorical variables by using the chi-squared tests. The average marginal  
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35 175 effect (AME)<sup>15</sup> was used to compare RH vs OH and RH vs LH on costing outcomes at  
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37 176 intervention, 30 days, 90 days and 365 days. This approach adjusted for patient age, ethnicity,  
38  
39 177 IMD rank, Charlson Comorbidity Index, year of procedure and whether a patient received  
40  
41 178 cancer treatment following the intervention (for further details see Appendix Table A3) by  
42  
43 179 fitting Generalised Linear Models (GLMS). The Modified Park Test & Pregibon's Link Test<sup>16</sup>  
44  
45 180 were used to ensure the most efficient model structure was used to model the costs. All  
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47 181 statistical analyses were performed using Stata 15®.  
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### 53 182 ***Patient and Public Involvement***

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56 183 There was no patient or public involvement in the study planning or design.  
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## 185 RESULTS

186 A total of 35,304 procedures were performed, 18,604 (52.7%) LH, 1,801 (5.1%) RH, 14,291  
187 (40.5%) OH and 608 (1.7%) VH. The proportion of MIS cases increased significantly overtime  
188 each year from 46.6% in 2012/13 to 68.7% in 2016/17 ( $p<0.001$ ). This was primarily due to an  
189 increase in LH of 15.8% (44.7% to 60.5%), but there was also a 6.2% increase (2.0% to 8.2%)  
190 in the number of RH performed when comparing 2012/13 to 2016/17 as a proportion of all  
191 surgeries performed each year. Consequently, the number of OH cases decreased significantly  
192 overtime ( $p<0.001$ ) from 53.4% in 2012/13 to 31.3% in 2016/17 of cases in that year.

193 Table 1 presents the patient characteristics of the surgical approaches LH, RH and OH. Most  
194 cases were performed at high volume providers ( $>220$  cases/year) with 72.4% for RH, 62.1%  
195 for LH and 60.9% for OH being undertaken at these providers (Table 1). As previously  
196 described, there was a significant difference in the social/ethnic characteristics of the patients  
197 undergoing MIS as compared to OH within this cohort of patients<sup>8</sup>. The characteristics of the  
198 RH population differed to patients undergoing LH; with a significantly higher percentage of  
199 RH patients having any co-morbidity from our defined list than LH (68.2% vs 64.0%,  $p<0.001$ ),  
200 more specifically the comorbidities of diabetes, hypertension and obesity all being higher  
201 proportion in RH cohort than LH cohort.

### 202 *Short-term costs by approach*

203 The short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach are  
204 presented in Table 2. LH was associated with the lowest mean cost at the intervention (£3069),  
205 30 (£3083), 90 (£3111) and 365 (£3169) days following the procedure. The mean cost for RH  
206 was significantly less than OH at all the time points ( $p<0.001$  for all). The average marginal  
207 effect (AME) for RH versus OH, controlling for patient characteristics, also showed a  
208 significant difference for RH over OH with the difference in cost increasing when comparing

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3 209 the unadjusted and AME value ( $p < 0.001$  for all). Comparing RH and LH short-term costs, LH  
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5 210 costs were significantly lower for the unadjusted and AME differences ( $p < 0.001$  for all). The  
6  
7 211 AME differences in cost between RH and LH were lower compared to the unadjusted  
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9 212 differences (e.g., AME difference of £108 vs. unadjusted difference of £260 at intervention).

### 213 ***High-Cost and Low-Cost Patient Comparison***

214 Assessing the top 5% highest cost (HC) patients of each approach (LH:  $n=336$ ; OH:  $n=593$ ,  
215 RH:  $n=27$ ) and comparing to the low-cost (LC) cohort, which was set at less than or equal to  
216 the median cost of the surgery (LH:  $n=12,913$ ; OH:  $n=9,021$ , RH:  $n=812$ ). The patients in the  
217 HC group were significantly older in all the routes of surgery (LH: 69.0 vs 65.7 years, OH:  
218 68.8 vs 65.1 years, RH: 67.5 vs 65.5 years:  $p < 0.001$  for all). The HC cohort contained a higher  
219 percentage of patients from the lower socioeconomic groups (IMD Rank: 16637 vs 17287,  
220  $p < 0.001$ ) and patients from ethnic minority groups (29.6% vs 19.2%,  $p < 0.001$ ) as compared to  
221 the LC cohort. Patients in the HC cohort also had significantly greater number of co-morbidities  
222 compared to the LC cohort (CCI 1.82 vs 1.41 and any comorbidity 71.0% versus 63.9%  
223  $p < 0.001$  for all). The length of hospital stay was significantly longer in the HC cases compared  
224 to the LC group (RH: 11.22 vs 1.84 days; LH: 11.42 vs 2.03 days; OH: 20.82 vs 3.71 days;  
225  $p < 0.001$  for all). Although the rate of complications was greater in the HC compared to the LC  
226 cohort (RH: 55.6% vs 14.0%; LH: 61.0% vs 16.2%; OH: 71.5% vs 19.1%;  $p < 0.001$  for all),  
227 the rate was significantly lower with RH as compared to OH in both the HC and LC groups  
228 (HC: 55.6% vs 71.5%,  $p = 0.075$ ; LC: 14.0% vs 19.1%,  $p < 0.001$ ).

### 229 ***Patient Characteristics and Costs***

230 Patient characteristics, age and CCI, were associated with increasing costs for almost all routes  
231 of surgery at intervention, and 365 days following the procedure (Table 3). Assessing the age  
232 categories showed the costs at intervention were very similar for the <50 years, 50-59 years

233 and 60-69 years groups but gradually increased for each of the higher age groups. There was  
234 an increasing difference between the MIS and OH costs with rising age with the difference  
235 between MIS and OH for Age <50 being £258 increasing to a difference of £653 for Age >90  
236 years population. RH 365-day costs were significantly lower ( $p<0.01$ ) than OH in all age  
237 categories except 60-69 & 90> years. Comparing CCI showed that CCI group  $\geq 3$  was  
238 associated with the greatest difference in costs with the difference at 365 days between CCI  
239 group 1 and CCI group  $\geq 3$  being £130 for RH, £174 for LH and £759 for OH (Table 3).

240 Overtime patients who underwent RH had increasing levels of co-morbidities, when using the  
241 CCI score, and have in recent years had a higher average CCI than LH in 2015/16-2016/17  
242 (Figure 1). Comparing the cost of LH and RH against CCI score, identified that the costs closely  
243 reflected the patients' CCI. In 2012/13 when the RH population had a lower CCI then the costs  
244 were less, however, since 2014/15 the patient population undergoing RH higher CCI score and  
245 this was associated with a rise in the costs of RH above that of LH (Figure 1).

### 246 *Hospital Characteristics and Costs*

247 When exploring the association between provider volume, MIS rate and surgical costs there  
248 was an association with the MIS rate and cost, i.e. the greater the MIS rate the lower the cost  
249 (Figure 2). Many of the highest volume providers had higher average costs than providers with  
250 less volume, however the patient population undergoing surgery at the high volume providers  
251 were significantly older and had a higher CCI compared to the lower volume providers (Age:  
252 66.2 vs 65.6 years,  $p<0.001$ ; CCI: 1.47 vs 1.43,  $p<0.001$ ). The majority of the highest volume  
253 providers had MIS rates between 50% to 90% and the relationship held for high volume  
254 providers with average costs decreasing as MIS rates increased for the year 2016/17.

## 255 **DISCUSSION**

### 256 *Main findings*

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3 257 In this study, we have performed an in-depth analysis of real-world data and have identified  
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5 258 financial benefits for MIS as compared to OH for EC. We have demonstrated that LH has the  
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8 259 lowest mean cost at intervention and that costs increased with increasing patient age. In keeping  
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10 260 with other studies, we have also shown that OH, although attracting the lowest operative  
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12 261 consumable costs, had the greatest overall financial cost, even significantly higher than RH.  
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14 262 We have also identified that although the cost of RH is greater than LH, patients undergoing  
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16 263 RH have different characteristics compared to women having LH in recent years, and that cost  
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18 264 of surgery appears to be influenced by level of patients' co-morbidities and not the route of  
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20 265 surgery alone.  
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23  
24 266 There will always be a proportion of cases that have to be performed OH due to contra-  
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26 267 indications/complications with MIS, which will inevitably attract higher costs due to their  
27  
28 268 complexity, but this can be reduced to low levels<sup>17</sup>. The significantly higher complication/re-  
29  
30 269 admission rate with OH have been reported previously<sup>8</sup> and in this study we have shown that  
31  
32 270 even in the HC groups, the complication rate was higher with OH (71.5%) as compared to RH  
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34 271 (55.6%) and LH (61.0%). A longer recovery time may impact on patient and employment  
35  
36 272 costs, with greater loss of earnings and longer return to work or contribution to society activities  
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38 273 as compared to MIS. Korsholm et al.<sup>18</sup>, reported no significant difference in return to the labour  
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40 274 market or use of sickness benefits in a study from Denmark however, in their study robotic  
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42 275 surgery was associated with greater cost than both laparoscopic and open hysterectomy, unlike  
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44 276 this UK analysis. Allowing for a number of OH cases, the disparity in MIS uptake across  
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46 277 England<sup>8</sup> does indicate that there is room for improvement in increasing the proportion of MIS  
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48 278 cases and thereby benefitting both the patient and the healthcare economy.  
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55 279 The primary argument used against the widespread use of RH, rather than LH, for EC is an  
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57 280 economic one<sup>6,19</sup>, since the clinical outcomes are reported to be comparable although, there is  
58  
59 281 a lack of randomised control trial data, particular in patients with a high BMI<sup>20</sup>. The HES data



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3 282 does confirm a cost advantage for LH over RH however, the two patient populations are not  
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5 283 directly comparable since there is a significant difference in the CCIs between the groups.  
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7 284 During 2012/13, when RH was only performed in a few selected centres, the majority of UK  
8  
9 285 robotic surgeons would still have been within the learning phase, and therefore likely to select  
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11 286 patients with less co-morbidities for RH. We have shown that during this time period the cost  
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13 287 of RH was less than LH. Increasing robotics experience appears to have led to the positive  
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15 288 selection of co-morbid patients, especially high BMI, for RH, and this is associated with rising  
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17 289 costs. Class III obesity and a rising number of patient co-morbidities are reported to attract  
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19 290 increased inpatient care costs due to increased medical rather than surgical complications  
20  
21 291 associated with undergoing surgery<sup>21,22</sup>. The selection of patients with a high-BMI for RH is  
22  
23 292 not unexpected given the reported ergonomic benefits for surgeons as compared to straight-  
24  
25 293 stick laparoscopy<sup>23</sup>, with less movements and muscle activity required to perform tasks<sup>24</sup>. RH  
26  
27 294 is not without issues due to the fixed console position<sup>25</sup>, however more extreme muscle  
28  
29 295 movements are required for laparoscopic procedures increase with rising BMI<sup>24</sup>, which is not  
30  
31 296 reported with robotics. The cost to the healthcare service of work-related musculoskeletal  
32  
33 297 symptoms in surgeons is of growing concern<sup>26</sup> and not considered in economic analyses such  
34  
35 298 as this study, however it is an additional cost that needs to be considered when calculating  
36  
37 299 service delivery costs.

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39  
40 300 What is clear from the data is that OH is the most costly route of surgery, a finding reported in  
41  
42 301 other healthcare settings<sup>27</sup>, not only in financial terms but more importantly for patient  
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44 302 complications and post-operative mortality<sup>8</sup>. The key focus therefore, rather than being  
45  
46 303 between LH or RH, should instead be on reducing the OH rate to a minimum. Although there  
47  
48 304 are only a few absolute contra-indications for OH, the number of cases that are performed  
49  
50 305 through open surgery is still high in some institutions and there has been much discussion how  
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52 306 this could be reduced through greater surgical training<sup>28</sup> or centralisation of cases to hospitals  
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3 307 and surgeons with high MIS rates<sup>29</sup>. A reduction in OH can also be achieved through reducing  
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5 308 the number of conversions from LH/RH to a minimum. A meta-analysis of observational  
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7 309 studies did show that the conversion rate of LH increased with BMI >40kg/m<sup>2</sup> more than for  
8  
9 310 RH, 6.5% (95% CI 4.3-9.9) versus 5.5% (95% CI 3.3-9.1), as compared to >30kg/m<sup>2</sup>, 7.0%  
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11 311 (95% CI 3.2-14.5) versus 3.8% (95% CI 1.4-9.9) respectively<sup>20</sup>. One reason for this may be the  
12  
13 312 lower intra-abdominal insufflation pressure often used with RH, typically 8mmHg, which has  
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15 313 been shown to be associated with lower post-operative pain and shorter hospital stay as  
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17 314 compared to a pressure 15mmHg<sup>30</sup>. Inability to tolerate Trendelenburg position was also  
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19 315 reported to be the indication for 31% of LH conversions but only 6% of RH conversions<sup>20</sup>. This  
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21 316 therefore raises the possibility as to whether cases should be selected for RH where there is  
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23 317 high risk of conversion due to Class III obesity or inability tolerate the pneumoperitoneum.  
24  
25 318 Further research is needed to compare the clinical outcomes and costs of LH and RH in matched  
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27 319 populations, for example BMI >40kg/m<sup>2</sup> or previous abdominal surgery, to investigate whether  
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29 320 differences reported in retrospective case series are confirmed. Such trials would determine  
30  
31 321 whether certain patient characteristics could be used to personalise the route of surgery in order  
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33 322 to maximise the potential benefit from MIS and reduce the rate of OH. Prospective randomised  
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35 323 controlled trials (RCT) are the gold standard study design however can be challenging to  
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37 324 perform and may be subject to many biases, including patient selection, if a surgeon has a  
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39 325 greater preference for one surgical modality over another. Also, RCTs can take many years to  
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41 326 complete accrual, for example LACC<sup>31</sup>, by which time the current robotic/laparoscopic  
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43 327 platforms may be obsolete. Instead, the use of real-world data in a propensity score matching  
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45 328 study may enable matching of key patient characteristics to give results in a more timely  
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47 329 manner<sup>32</sup>. The development and adoption of prognostic and risk-stratifying biomarkers in the  
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49 330 future may also inform decisions on the optimum route of surgery thereby enabling more  
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51 331 personalised management<sup>33-35</sup>.

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3 332 ***Strengths and limitations***  
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6 333 The key strength of the study is in the number of patients in which can be analysed by using  
7  
8 334 the HES database. This gives strength to the study's findings as it is representative of all  
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10 335 procedures via the NHS in England. Due to RH being a newer surgery approach the number of  
11  
12 336 patients is much lower compared to the other surgery approaches. In addition, we must consider  
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14 337 the impact of a learning curve of RH and that in the earlier years it may not been used to full  
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16 338 efficiency. As we had a number of years of the HES database we could analyse any potential  
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18 339 trends across surgical approaches and the year.  
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23 340 As we have previously described<sup>8</sup>, HES data does have limitations, primarily it only covers  
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25 341 NHS-funded care, the reliability of coding and lacks oncological details of stage/histology. A  
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27 342 limitation of the CCI calculated using the HES data is that people with no hospital attendance  
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29 343 12 months prior to intervention are classified as having no comorbidities instead of missing,  
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31 344 but as the NHS is free at the point of contact the HES database is extensive at capturing all  
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33 345 hospital reported comorbidities in England. There will be a proportion of patients with  
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35 346 advanced disease that require open surgery due to requiring a more extensive cytoreductive  
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37 347 procedure and HES data is not able to differentiate these cases from early-stage disease that is  
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39 348 being treated through open surgery. The analysis comparing LH and RH should however not  
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41 349 be impacted by stage of disease. In addition, there are limitations with the HES data with the  
42  
43 350 recording of magnitude of patient co-morbidities, in particular obesity since a numerical value  
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45 351 for BMI is not included and therefore the obesity classification could be applied to any patient  
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47 352 with a BMI >30kg/m<sup>2</sup>.  
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53 353 The capital and maintenance costs of RH have also not been included since these costs vary  
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55 354 dramatically across different healthcare settings and there would be a need to also included  
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57 355 similar costs for laparoscopic and open surgery. In addition, the robotic surgery equipment is  
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3 356 often utilised by a wide group of specialities in a hospital setting and it would be infeasible to  
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5 357 apply capital and maintenance costs to one surgery modality<sup>15</sup>.  
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8 358 ***Interpretation***  
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11 359 In conclusion, LH was associated with the lowest and OH the greatest mean cost per procedure.  
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13 360 Patient factors have an impact on the cost of MIS procedures and further research is needed to  
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15 361 compare the costs in matched populations of women undergoing LH and RH, since there  
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17 362 appears to be selection bias in the choice of procedure being performed.  
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20  
21 363 **Ethical approval:** The HES database is managed by the NHS Digital and is available for  
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23 364 research without ethical approval.  
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27 366 All the authors consent to publication  
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32 368 **Data availability:** Data analysed in this study is available through Hospital Episode Statistics  
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34 369 (HES)  
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37 370 **Conflicts of Interest:** EM and TI perform Da'Vinci robotic gynaecological surgery (Intuitive  
38  
39 371 Surgical) and are members of the British and Irish Association of Robotic Surgeons (BIARGS),  
40  
41 372 which is supported by Intuitive Surgical and other robotics/laparoscopic companies to hold  
42  
43 373 education/training events. EM has been awarded research grants from Intuitive Surgical and  
44  
45 374 Hope Against Cancer for unrelated studies, serves on advisory boards for Inivata and  
46  
47 375 GlaxoSmithKline and has received speaker fees from GlaxoSmithKline. TI has done two days  
48  
49 376 paid consultancy work for Medtronic. GM and AM from HCD Economics were funded by  
50  
51 377 Intuitive Surgical. None of the clinicians (EM, PS, TI) received funding from Intuitive Surgical  
52  
53 378 for this study. Intuitive Surgical did not have any involvement with the study design, data  
54  
55 379 analysis and writing of the manuscript. The authors declare no other potential conflict of  
56  
57 380 interest.  
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56 382 **Contributors:** EM, TI, GM and AM contributed to the conceptualisation and study design.7  
8 383 Data analysis and interpretation was performed by EM, TI, GM, AM and PS. Figures and tables9  
10 384 creation was performed by EM, GM and AM. All authors were involved in the writing or11  
12 385 review of the manuscript and approved the final version.13  
14  
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17 387 Hospital Episode Statistics Data via a Standard Extract Re-use Agreement issued by the Health18  
19 388 & Social Care Information Centre 2018.20  
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22  
23 389 **Figure 1: Intervention Cost & CCI Over Time**24  
25 390 The average cost and CCI of RH & LH over time.26  
27 391 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic  
28 392 hysterectomy, NHS = National Health Service)29  
30 393 **Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17**31  
32 394 The association between provider volume, MIS rate and surgical cost at intervention. Provider  
33 395 volume is represented by the size of the bubble with a larger bubble representing a higher  
34 396 provider volume.35  
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523 **Table 1. Clinical and Demographic Characteristics by the cohorts of hysterectomy approach**

Characteristics	Unadjusted Results							
	Laparoscopic Hysterectomy (N=18604)		Robotic Hysterectomy (N=1801)		MIS Hysterectomy (N=20405)		Open Hysterectomy (N=14291)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<b>NHS Year of surgery</b>								
2011/12*	1,108	6%	19	1%	1,127	6%	1,671	12%
2012/13	2,367	13%	104	6%	2,471	12%	2,829	20%
2013/14	2,824	15%	147	8%	2,971	15%	2,614	18%
2014/15	3,134	17%	253	14%	3,387	17%	2,361	17%
2015/16	3,118	17%	382	21%	3,500	17%	1,948	14%
2016/17	3,577	19%	483	27%	4,060	20%	1,852	13%
2017/18*	2,476	13%	413	23%	2,889	14%	1,016	7%
<b>Age, years</b>								
<50	1,033	6%	120	7%	1,153	6%	1,082	8%
50-59	3,937	21%	380	21%	4,317	21%	3,098	22%
60-69	6,522	35%	589	33%	7,111	35%	4,672	33%
70-79	5,160	28%	533	30%	5,693	28%	3,779	26%
80-89	1,846	10%	174	10%	2,020	10%	1,540	11%
90>	106	1%	5	0%	111	1%	120	1%
<b>Ethnicity</b>								
White	15,033	81%	1,420	79%	16,453	81%	11,117	78%
Asian	583	3%	66	4%	649	3%	499	3%
Black	231	1%	20	1%	251	1%	365	3%
Other	2,757	15%	295	16%	3,052	15%	2,310	16%
<b>Socio-Economic Group (IMD)</b>								



High	4,506	25%	643	37%	5,149	25%	3,291	23%
Intermediate	4,612	25%	403	23%	5,015	25%	3,387	24%
Low	4,548	25%	376	21%	4,924	24%	3,489	24%
Very Low	4,435	25%	333	19%	4,768	23%	3,703	26%
<b>Charlson Comorbidity Group</b>								
0	22	0%	1	0%	23	0%	13	0%
1	12,432	67%	1,159	64%	13,591	67%	8,405	59%
2	4,915	26%	514	29%	5,429	27%	4,535	32%
>=3	1,235	7%	127	7%	1,362	7%	1,338	9%
<b>Region</b>								
Greater London	2,529	14%	319	18%	2,848	14%	2,184	15%
Yorkshire	1,501	8%	270	15%	1,771	9%	1,220	9%
West Midlands	1,747	9%	154	9%	1,901	9%	1,672	12%
South West	2,676	14%	75	4%	2,751	13%	1,348	9%
South East	1,746	9%	339	19%	2,085	10%	1,451	10%
North West	2,628	14%	281	16%	2,909	14%	2,550	18%
North East	1,264	7%	138	8%	1,402	7%	432	3%
Home Counties	1,095	6%	31	2%	1,126	6%	912	6%
East Midlands	1,485	8%	165	9%	1,650	8%	1,003	7%
East	1,922	10%	4	0%	1,926	9%	1,497	10%
<i>Missing</i>	11	0%	25	1%	36	0%	22	0%
<b>Provider Volume</b>								
High	11,423	62%	1,302	72%	12,725	62%	8,703	61%
Intermediate	6,653	36%	487	27%	7,140	35%	5,102	36%
Low	279	2%	9	1%	288	1%	191	1%
Very Low	36	0%	0	0%	36	0%	58	0%
<i>Missing</i>	213	1%	3	0%	216	1%	237	2%

524 \*NHS Year 2011/12 &amp; 2017/18 not full year

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526 **Table 2. Short-term costs of intervention, 30 days, 90 days and 365 days by surgical approach**

	Mean Cost in £ (SD)			Difference RH vs OH				Difference RH vs LH			
	RH (N =1353)	OH (N=12379)	LH (N=15666)	Unadjusted Difference (£)	P Value	AME (£) *	P Value	Unadjusted Difference (£)	P Value	AME (£) *	P Value
<b>At Intervention</b>	3329 (713)	3349 (1318)	3069 (676)	-20	<0.001	-197	<0.001	260	<0.001	108	<0.001
<b>At 30 days</b>	3334 (722)	3379 (1395)	3083 (721)	-45	<0.001	-220	<0.001	251	<0.001	98	<0.001
<b>At 90 days</b>	3357 (761)	3424 (1468)	3111 (826)	-67	<0.001	-241	<0.001	246	<0.001	89	<0.001
<b>At 365 days</b>	3417 (906)	3533 (1687)	3169 (984)	-116	<0.001	-273	<0.001	248	<0.001	94	<0.001

527 \*AME adjusted for Year, Age, Socioeconomic Status (IMD Rank), Charlson Comorbidity, Ethnicity, Cancer Tx

528 Notes:

529 RH vs OH: We see that the average marginal effect is greater than the actual difference between RH and OH when we control for covariates

530 RH vs LH: We see the average marginal effect is less than the actual difference between RH and LH when we control for covariates

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6/bmjopen-2020-045888 on 13 May 2021. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

538 **Table 3. Mean Cost at intervention and 365 days by CCI/Age for each approach**

	LH			RH			MIS			OH	
	N	Mean (SD)	P-Value*	N	Mean (SD)	P-Value*	N	Mean (SD)	P-Value*	N	Mean (SD)
<b>Age Groups (Costs at Intervention)</b>											
<50	860	£3032 (616)	<0.001	90	£3284 (942)	0.783	950	£3056 (657)	<0.001	921	£3314 (1325)
50-59	3336	£3025 (558)	<0.001	293	£3258 (593)	0.967	3629	£3044 (565)	<0.001	2687	£3259 (1033)
60-69	5522	£3053 (657)	<0.001	436	£3357 (819)	0.089	5958	£3075 (675)	<0.001	4077	£3283 (1173)
70-79	4328	£3101 (732)	<0.001	398	£3343 (600)	0.052	4726	£3121 (725)	<0.001	3255	£3419 (1406)
80-89	1533	£3149 (777)	<0.001	134	£3385 (716)	0.041	1667	£3168 (774)	<0.001	1338	£3546 (1782)
90>	87	£3215 (1311)	0.023	<10	£3454 (687)	0.461	89	£3220 (1298)	0.023	101	£3855 (2425)
<b>CCI Groups (Costs at Intervention)</b>											
0	21	£3060 (292)	0.156	<10	£3939 (0)	-	22	£3100 (341)	0.078	12	£2968 (0)
1	10526	£3038 (616)	<0.001	887	£3319 (763)	0.010	11413	£3060 (633)	<0.001	7369	£3247 (994)
2	4126	£3126 (777)	<0.001	377	£3337 (607)	0.051	4503	£3143 (767)	<0.001	3875	£3412 (1375)
>=3	993	£3166 (806)	<0.001	88	£3391 (614)	<0.001	1081	£3184 (794)	<0.001	1123	£3808 (2421)
<b>Age Groups (Costs at 365 days)</b>											
<50	860	£3136 (900)	<0.001	90	£3287 (945)	0.005	950	£3150 (905)	<0.001	921	£3615 (1821)
50-59	3336	£3111 (903)	<0.001	293	£3274 (612)	0.005	3629	£3125 (884)	<0.001	2687	£3399 (1373)
60-69	5522	£3144 (922)	<0.001	436	£3476 (1091)	0.638	5958	£3169 (940)	<0.001	4077	£3449 (1503)
70-79	4328	£3219 (1103)	<0.001	398	£3468 (836)	0.008	4726	£3240 (1086)	<0.001	3255	£3607 (1806)
80-89	1533	£3256 (1017)	<0.001	134	£3477 (925)	0.003	1667	£3274 (1011)	<0.001	1338	£3776 (2169)
90>	87	£3252 (1350)	0.003	<10	£3454 (687)	0.200	89	£3257 (1337)	0.003	101	£4175 (2774)
<b>CCI Groups (Costs at 365 days)</b>											
0	21	£3074 (294)	0.106	<10	£3939 (0)	-	22	£3114 (341)	0.054	12	£2968 (0)
1	10526	£3126 (891)	<0.001	887	£3358 (827)	0.323	11413	£3144 (888)	<0.001	7369	£3390 (1368)
2	4126	£3249 (1160)	<0.001	377	£3538 (1088)	0.148	4503	£3273 (1157)	<0.001	3875	£3629 (1745)
>=3	993	£3299 (1097)	<0.001	88	£3488 (747)	<0.001	1081	£3315 (1073)	<0.001	1123	£4148 (2832)

\*Significance test were carried out against the OH category within each age/CCI group for the approaches LH, RH and MIS

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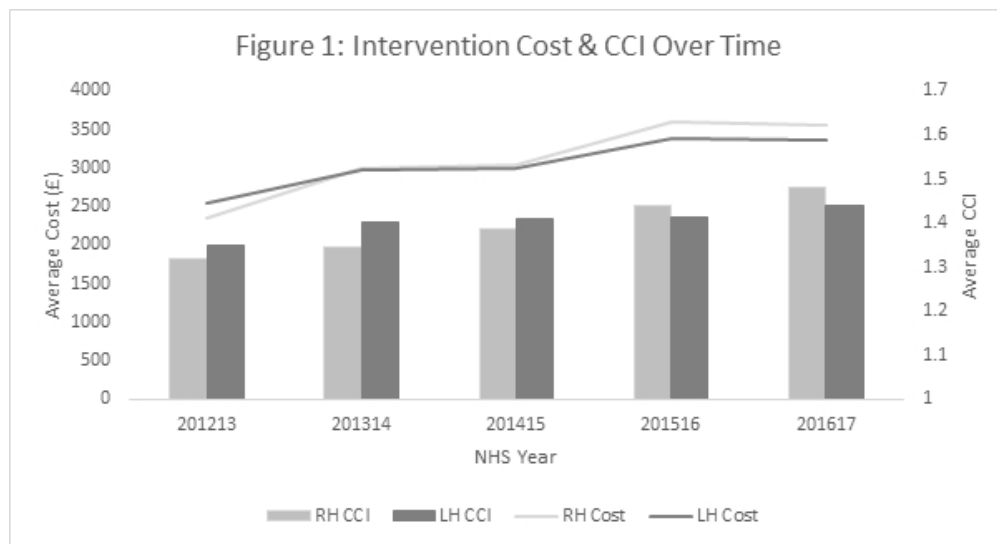


Figure 1: Intervention Cost & CCI Over Time  
 The average cost and CCI of RH & LH over time.  
 (CCI = Charlson Comorbidity Index, LH = laparoscopic hysterectomy, RH = robotic hysterectomy, NHS = National Health Service)

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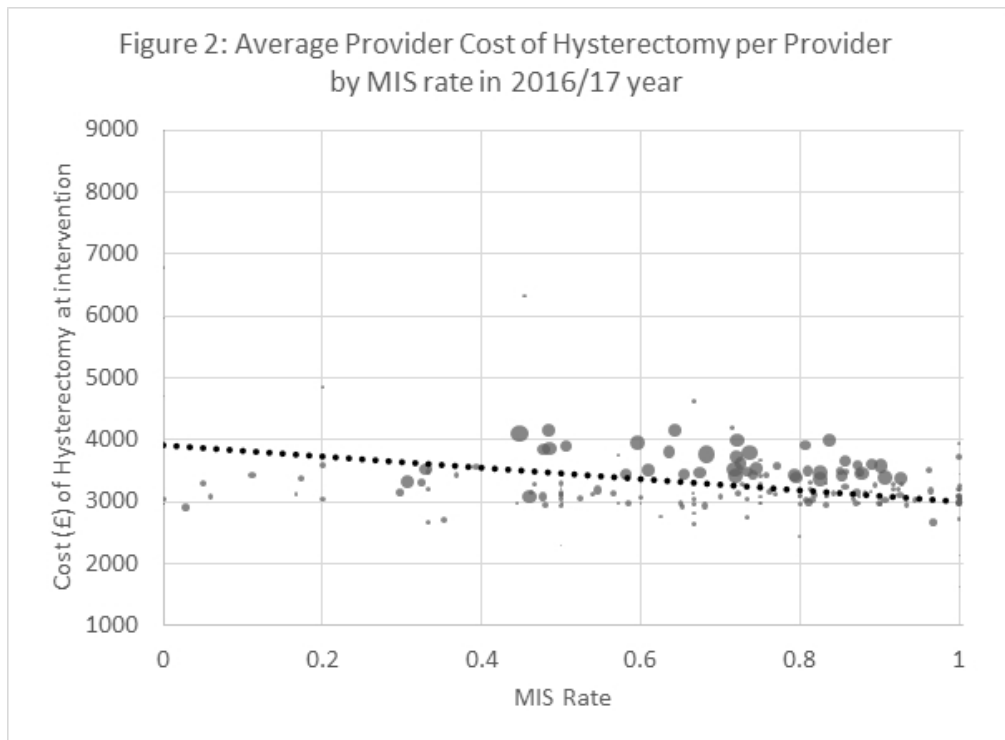


Figure 2: Average Provider Cost of Hysterectomy per Provider by MIS rate in 2016/17  
 The association between provider volume, MIS rate and surgical cost at intervention. Provider volume is represented by the size of the bubble with a larger bubble representing a higher provider volume.

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## Appendix Tables:

Table A1- Cohort Selection ICD-10 & OPCS-4.7 Codes

Table A1: Cohort Selection

Category	ICD-10 / OPCS-4.7
<b>Hysterectomies</b>	Procedures with: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9
<b>Endometrial/uterine carcinoma or endometrial carcinoma in situ</b>	Patients must have as primary diagnosis: C540, C541, C542, C543, C548, C549, C55X, D070
<b>Laparoscopic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9
<b>Robotic hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.3
<b>Open hysterectomy</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Vaginal hysterectomy</b>	Any procedures with one of: Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And without any: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9 Y75.3
<b>Minimally Invasive Surgery</b>	Any procedures with one of: Q07.1, Q07.2, Q07.3, Q07.4, Q07.5, Q07.8, Q07.9, Q08.1, Q08.2, Q08.3, Q08.8, Q08.9 And with one of: Y75.1, Y75.2, Y75.5, Y75.8, Y75.9, T43.9, Y75.3

Table A2 – Other complications OPCS-4.7 codes assessed

Table A2: Complication classification<sup>a</sup>

Category	ICD-10 / OPCS-4.7
<b>Gastrointestinal complications</b>	A090 I898 K228 K250 K252 K254 K256 K260 K261 K262 K264 K265 K266 K270 K272 K274 K276 K280 K282 K284 K286 K290 K450 K560 K565 K566 K567 K625 K631 K638 K660 K720 K729 K85 K913 K918 K919 K92 S360 K61 N824
<b>Wounds</b>	D649 K603 K604 K605 K632 K829 K832 L89 T813 T815 T343 T453 T793
<b>Infections</b>	A40 A41 A49 B95 B96 K630 K65 L03 L04 N10 N12 N151 N159 N300 N309 N390 R788 T793 T802 T814 T816 T827 T836 T857
<b>Uteric Injury Complication</b>	N133 N139 N17 N19 N280 N312 N990 N991 N998 N999 R32 R33 S360 N12 N151 N159 N300 N309 N390 N360 S371 N131 N821
<b>Haemorrhage</b>	T810 S35 D65
<b>Cardiovascular disorders</b>	I21 I46 I48 I49 I50 I74 I80 I81 I82 I950 I952 I959 I978 I979 R57 T801 T811 T817 T827
<b>Pulmonary complications</b>	J80 J81 J90 J91 J93 J955 J958 J959 J960 J969 J981 R060 R09 I26 J100 J110 J12 J13 J14 J15 J16 J17 J18 J690 J85 J86
<b>Neurological disorders</b>	F05 F13 F15 F19 G45 G46 G569 G81 G82 G83 G931 G936 G970 G971 G978 G979 I63 I65
<b>Other</b>	T882 T790 T800 E15 E272 E86 E87 R798 T812 T818 T888 T792

<sup>a</sup> Adapted from Ma C, et al. Postoperative complications following colectomy for ulcerative colitis: A validation study. BMC Gastroenterol 2012; 12:39.

Table A3: Cancer Treatment OPCS 4.7 Codes excluded for cost analysis

Category	Specific Code	Sub Category
Chemotherapy	X70.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 1
	X70.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 2
	X70.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 3
	X70.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 4
	X70.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 5
	X70.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X70.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 1-5
	X71.1	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 6
	X71.2	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 7
	X71.3	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 8
	X71.4	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 9
	X71.5	Procurement of drugs for chemotherapy for neoplasm for regimens in Band 10
	X71.8	Other specified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X71.9	Unspecified procurement of drugs for chemotherapy for neoplasm in Bands 6-10
	X72.1	Delivery of complex chemotherapy for neoplasm including prolonged infusional treatment at first attendance
	X72.2	Delivery of complex parenteral chemotherapy for neoplasm at first attendance
	X72.3	Delivery of simple parenteral chemotherapy for neoplasm at first attendance
	X72.4	Delivery of subsequent element of cycle of chemotherapy for neoplasm
	X72.8	Other specified delivery of chemotherapy for neoplasm
	X72.9	Unspecified delivery of chemotherapy for neoplasm
	X73.1	Delivery of exclusively oral chemotherapy for neoplasm
	X73.8	Other specified delivery of oral chemotherapy for neoplasm
	X73.9	Unspecified delivery of oral chemotherapy for neoplasm
	X74.1	Cancer hormonal treatment drugs Band 1
	X74.2	Cancer supportive drugs Band 1
	X74.8	Other specified other chemotherapy drugs
	X74.9	Unspecified other chemotherapy drugs
Radiotherapy	X65.1	Delivery of a fraction of total body irradiation
	X65.2	Delivery of a fraction of intracavitary radiotherapy
	X65.3	Delivery of a fraction of interstitial radiotherapy
	X65.4	Delivery of a fraction of external beam radiotherapy NEC
	X65.5	Oral delivery of radiotherapy for thyroid ablation
	X65.6	Delivery of a fraction of intraluminal brachytherapy
	X65.7	Delivery of radionuclide therapy NEC
	X65.8	Other specified radiotherapy delivery
	X65.9	Unspecified radiotherapy delivery
	X67.1	Preparation for intensity modulated radiation therapy
	X67.2	Preparation for total body irradiation
	X67.3	Preparation for hemi body irradiation
	X67.4	Preparation for simple radiotherapy with imaging and dosimetry
	X67.5	Preparation for simple radiotherapy with imaging and simple calculation
	X67.6	Preparation for superficial radiotherapy with simple calculation
X67.7	Preparation for complex conformal radiotherapy	
X67.8	Other specified preparation for external beam radiotherapy	



	X67.9	Unspecified preparation for external beam radiotherapy
	Y92.1	Technical support for preparation for radiotherapy
	Y92.2	Other specified support for preparation for radiotherapy
	Y92.3	Unspecified support for preparation for radiotherapy
Brachytherapy	X68.1	Preparation for intraluminal brachytherapy
	X68.2	Preparation for intracavitary brachytherapy
	X68.3	Preparation for interstitial brachytherapy
	X68.8	Other specified preparation for brachytherapy
	X68.9	Unspecified preparation for brachytherapy
	Y35.4	Introduction of radioactive substance into organ for brachytherapy NOC
	Y36.4	Introduction of non-removable radioactive substance into organ for brachytherapy NOC
	Y89.1	High dose rate brachytherapy treatment
	Y89.2	Pulsed dose rate brachytherapy treatment
	Y89.8	Other specified brachytherapy
	Y89.9	Unspecified brachytherapy

**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies**

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9 9 NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9 (Table 1) 9 (Table 1) 9
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11 9-11 NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12-14
<b>Limitations</b>			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-15
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).