Repeated intermittent ulipristal acetate in the treatment of uterine fibroids: a cost-effectiveness analysis

Supplementary material

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Quality of life decrements

Table 1: UPA short-term adverse event risk, quality of life decrements, and cost

	Monthly risk of AE[1]	Quality of life decrement	Cost (£)	Cost source
Acne	0.15%	-0.062[2]	45.23	1 GP visit and Dalacin T[3;4]
Anaemia	0.13%	-0.110[5]	1375.14	SA04K[6]
Anxiety	0.13%	-0.161[7]	181.89	AB11Z[6]
Fatigue	0.18%	-0.115[8]	0.00	Assume no cost
Headache	1.27%	0 (Assumption)	0.00	Assume no cost
Hot flushes	0.72%	-0.060[9]	38.00	1 GP visit[4]
Hypertension	0.11%	0 (Assumption)	759.13	EB04Z[6]
Increase creatine phosphokinase	0.13%	0 (Assumption)	0.00	Assume no cost
Influenza	0.29%	-0.010[10]	53.41	1 GP visit and oseltamivir[3;4]
Nasopharyngitis	0.20%	-0.010[10]	53.41	Assume influenza
Nausea	0.20%	-0.130[8]	0.97	Metoclopramide[3]
Pain (breast, pelvic, abdominal, back)	0.85%	-0.014[11]	468.37	FZ90B[6]
Vaginal discharge	0.18%	0 (Assumption)	0.00	Assume no cost
Vertigo	0.15%	-0.130[8]	42.26	1 GP visit and Cinnarizine[3;4]
Weight gain	0.11%	-0.099[12]	0.00	Assume no cost

Table 2: BSC short-term adverse event risk, quality of life decrements, and cost

	Monthly risk of AE[13]	Quality of life decrement	Cost (£)	Cost source
Headache	1.06%	0 (Assumption)	0.00	Assume no cost
Pain, discomfort, or aches	2.71%	-0.060[9]	468.37	FZ90B[6]
Pyrexia	1.06%	-0.010[10] (Assume influenza)	0.00	Assume no cost

Table 3: Surgery short-term adverse event risk, quality of life decrements, and cost

	Risk of adverse event per surgical procedure					Quality of life decrement	Cost (£)	Cost source
	AH[14]	LH[14]	VH[14]	Myo (all) [15]	UAE[15]			
Bowel obstruction				1.37%		-0.200[16]	797.80	FZ51Z[6]
Febrile event	2.50%	1.40%	0.90%			0 (Assumption)	0.00	Assume no cost
Fibroid expulsion					1.35%	-0.014[11] (Assume pain)	19.10	MA31Z[6]
Groin haematoma					2.70%	0 (Assumption)	0.00	Assume no cost
Haemorrhage	8.30%	5.70%	4.40%	1.37%		-0.198[17]	451.10	FZ38P[6]
Ileus				1.37%		-0.200[16]	38.00	1 GP visit[3]
Pelvic infection, haematoma or abscess	0.80%	3.20%	2.20%			-0.195[18]	452.00	WA09C[6]
Pneumonia				1.37%		-0.010[10] (Assume influenza)	366.19	SA04L[6]
Post embolization syndrome					8.11%	-0.144[8;11] (Assume pain+nausea)	469.34	Assume pain plus nausea
Pulmonary embolus				1.37%		-0.018[19]	235.47	DZ09F[6]
Sepsis				1.37%	1.35%	-0.120[20]	1 851.98	WA03C[6]
UTI	2.20%	0.70%	1.50%	10.96%		-0.070[21]	430.00	LA04S[6]
Urticaria					1%	0 (Assumption)	0.00	Assume no cost
Wound infection	2.40%	1.50%	0.90%			-0.195[18]	452.00	WA09C[6]

AH: Abdominal hysterectomy; LH: Laparoscopic hysterectomy; VH: Vaginal hysterectomy; Myo: Myomectomy; UAE: Uterine artery embolisation

Table 4: Quality of life decrements due to persistent complications (following hysterectomy)

	Quality of life decrement	Comment
Pain	-0.014[11]	Assuming abdominal pain
Hot flushes	-0.060[9]	
Fatigue	-0.115[8]	
Urinary problems	-0.070[21]	Assume urinary tract infection
Abdominal distention	-0.090[22]	Assume dyspepsia
Insomnia	-0.115[8]	Assume fatigue
Housework problems	-0.065[23]	
Anxiety	-0.161[7]	
Vaginal irritation and pruritus	-0.014[11]	Assuming pain

Extrapolation of pain and bleeding

In PEARL I and IV, pain and bleeding were measured at fixed intervals, and were extrapolated according to the following methods: In the BSC arm, the model imputes values between bleeding and pain observations by assuming a linear relationship until the last observation, where all following dates are assumed to be equal to the last observation. Similarly for pain in the UPA arm, a linear relationship between the observations was used. Bleeding imputation for UPA differed from that of BSC due to the timing of observations, which occurred one month into the treatment break. Following that observation, it was estimated from trial data that PBAC increased by 50 from the end of the first month of treatment break to the second, when UPA treatment was reinitiated. Using PBAC at the initiation date as a reference, trial data for UPA in PEARL I and II were used to measure the percentage decrease in bleeding in each month on active treatment.

Phase II refers to the long term treatment pattern where the treatment break was extended to six months.

Figure 1: UPA PBAC pattern including extrapolation

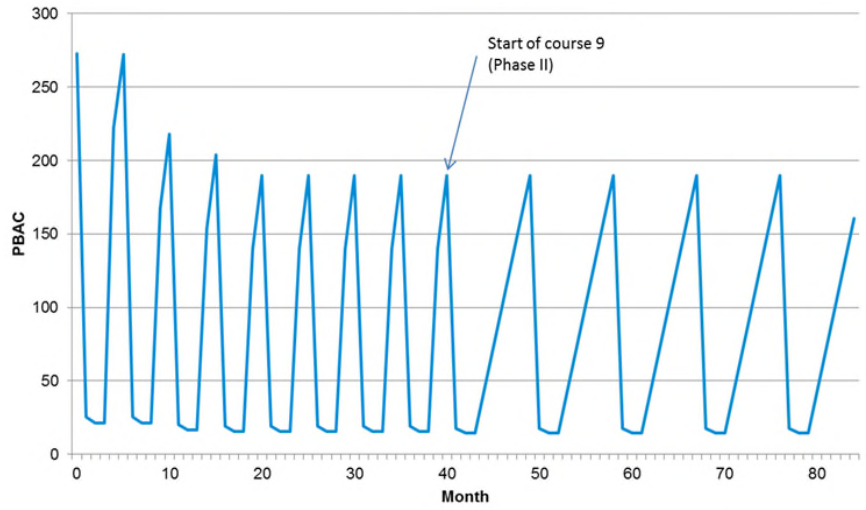
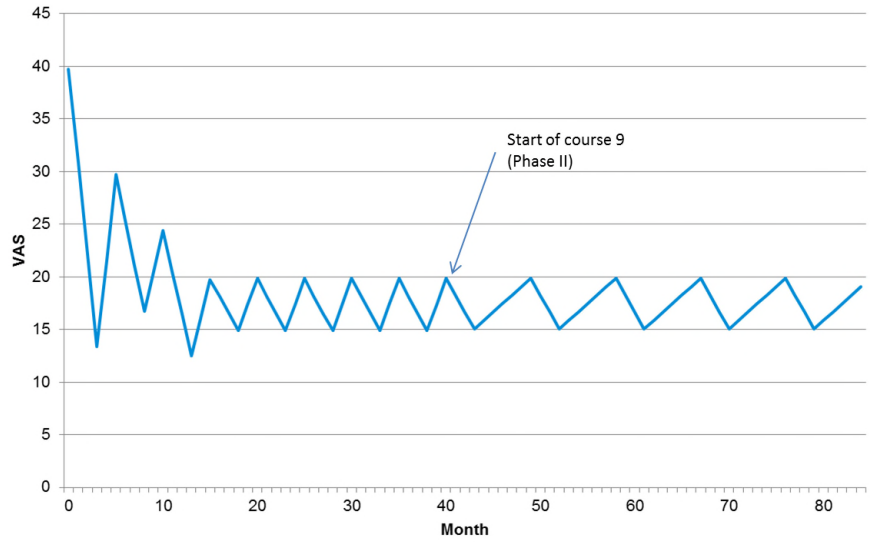


Figure 2: UPA VAS pattern, including extrapolation



Calculation of BSC withdrawal rate to surgery

The calculation of withdrawals to surgery from BSC was based on patients included in the observational PREMYA study[24,25]. There were 1139 patients that received no treatment, iron supplements, or NSAIDs prior to beginning PREMYA, corresponding to the BSC patient group. Of these patients, 142 received a uterine fibroid related surgery before the start of PREMYA. The average time between previous diagnosis of the 1139 patients and the beginning of PREMYA was 26.6 months, which is interpreted as the average time at risk of all 1139 patients. The percentage of patients receiving a surgery following a uterine fibroid diagnosis was calculated as 142 divided by 1139, equal to 12.5%. This risk was converted from 26.6 months to an annual risk assuming constant rates of surgery over time[26], to give the withdrawal rate for patients treated with BSC to surgery, equal to 5.83%.

Calculation of UPA withdrawal rate to surgery

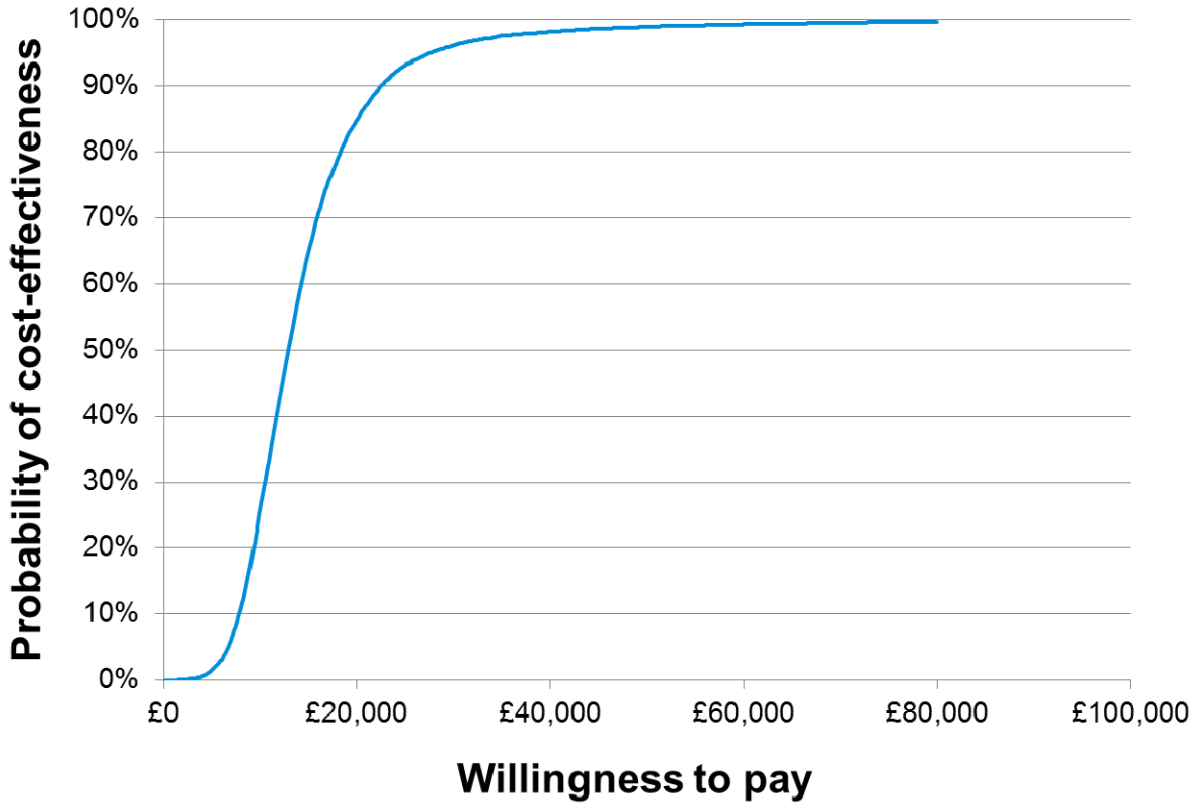
The cumulative UPA bleeding levels during course four were divided by the cumulative bleeding while on treatment with BSC during the same time period. The resulting calculation shows that UPA patients bled at a rate of 40.8% of BSC patients, and therefore it was assumed that UPA patients withdraw to surgery at a rate equal to 40.8% of BSC patients following course 4.

Probabilistic sensitivity analysis

Table 5: Distributions used for major parameter categories

Variable characteristic	Distribution used	Reason
Cost	Gamma	Positive, bounded at 0
Utility	Beta	Bounded between 0 and 1
Disutility	Negative gamma	Bounded between -∞ and 0
Risk	Beta	Bounded between 0 and 1
Proportion not relative to other parameters	Beta	Bounded between 0 and 1
Proportion relative to other parameters	Dirichlet	Draws must sum to given value (i.e. 100%)
Duration	Gamma	Positive, bounded at 0
Resource usage	Gamma	Positive, bounded at 0

Figure 3: Probability that UPA is cost-effective given increasing willingness to pay for a QALY

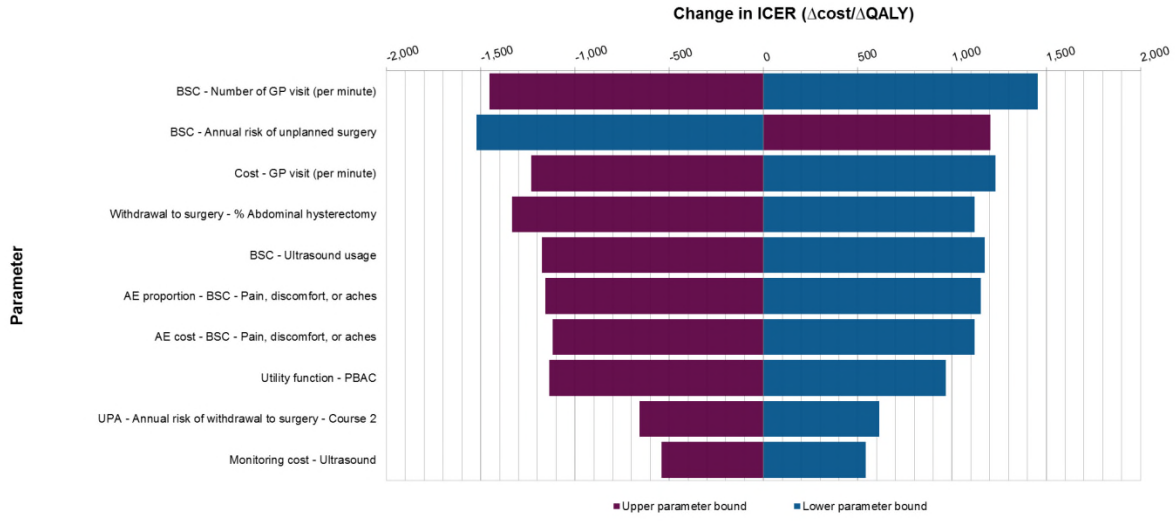


Deterministic sensitivity analysis (DSA)

In order to address the model's sensitivity to each parameter, the model's parameters are varied individually by +/- 10%. The results are presented in the form of a tornado diagram where the ten parameters with the largest influence on the ICER are included.

The results of the DSA should be interpreted in the context of the methodology of used – that is, each input parameter is varied individually. Changing a parameters value by 10% increases or decreases the ICER by a certain amount, showing the model's sensitivity to this parameter. It is not always clear whether a 10% change is realistic, and therefore the DSA may not always result in a realistic change in the ICER.

Figure 4: Deterministic sensitivity analysis (DSA): +/-10% parameter variation



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