An observational cohort study of health outcomes and costs associated with early pregnancy assessment units in the UK

Edna Keeney1*, Maria Memtsa2, Venetia Goodhart2, Davor Jurkovic2, Gareth Ambler3, Nazim Khan4 and Jeff Round5,6

Abstract
Background: The objective of this study was to assess the impact of consultant presence, volume of patients seen and weekend opening on the health and cost-related outcomes associated with different Early Pregnancy Assessment Unit (EPAU) configurations.

Methods: This was an observational study with a prospective cohort design. Six thousand six hundred six pregnant women (16 years of age and over) attending EPAUs because of suspected early pregnancy complications were recruited from 44 EPAUs across the UK. The main outcome measures were quality of life, costs, and anxiety.

Results: Costs, quality of life and anxiety scores were similar across configurations with little evidence to suggest an impact of consultant presence, weekend opening or volume of patients seen. Mean overall costs varied from £92 (95% CI £85 - £98) for a diagnosis of normally developing pregnancy to £1793 (95% CI £1346 - £2240) for a molar pregnancy. EQ-5D-5L score increased from 0.85 (95% CI 0.84–0.86) at baseline to 0.91 (95% CI 0.90–0.92) at 4 weeks for the 573 women who completed questionnaires at both time points, largely due to improvements in the pain/discomfort and anxiety/depression dimensions. 78% of women reported a decrease in their anxiety score immediately following their EPAU appointment.

Conclusions: EPAU configuration, as specified in this study, had limited impact on any of the outcomes examined. However, it is clear that care provided in the EPAU has a positive overall effect on women's health and emotional well-being, with significant improvements in EQ-5D and anxiety shown following an EPAU visit.

Keywords: Early pregnancy, Cohort study, Cost-effectiveness, Quality of life

Background
Complications in early pregnancy are common and account for the largest proportion of emergency work performed in gynaecology departments across the UK [1]. ‘Early pregnancy complications’ is a broad term that encompasses all types of pregnancy loss in the first 12 weeks of gestation (miscarriage, ectopic pregnancy, trophoblastic disease), as well as maternal complications such as hyperemesis gravidarum. Indicatively, it is estimated that, in the UK, per annum, there are 1,000,000 pregnancies, of which, at least 200,000 result in a miscarriage, and, at least 10,000 in an ectopic pregnancy (2007 CEMACH).

In the UK, women with suspected early pregnancy complications are mostly cared for in Early Pregnancy Assessment Units (EPAUs), specialist organisational structures, unique to the National Health Service...
(NHS). EPAUs aim to provide a dedicated, centralised outpatient service which includes clinical assessment, ultrasound, and laboratory investigations in an attempt to streamline and improve the quality of care for women that experience pain and/or bleeding in early pregnancy.

The number of EPAUs in NHS hospitals has increased exponentially since 1991, when Bigrigg and Read [2] first reported that the introduction of an EPAU at their local hospital resulted in improved quality of care and cost savings. EPAUs are reportedly associated with shortening of the time taken to reach the correct diagnosis as well as a reduction in the number of hospital admissions for women with suspected early pregnancy complications [2]. According to the Association of Early Pregnancy Units (AEPU), there are currently over 200 operational EPAUs in acute NHS hospital trusts in the UK [3]. However, the current paucity of evidence regarding how EPAUs should be organised has led to considerable variation amongst units across the country in the levels of access to their services and the levels of care they provide.

As hospital care is the most expensive element of the health service [4], healthcare providers, especially in cost-constrained systems, have to manage resources carefully. Previous studies have shown that inpatient admissions are significantly reduced when consultants are available to review patients in acute clinical settings, such as emergency departments and medical assessment units [5, 6]. Access to ultrasound diagnostic services provided by the EPAU is essential for the safe and effective management of women with early pregnancy complications. As such, if access to the EPAU is limited, it is likely that the number of precautionary admissions, in particular over the weekend, would be increased until potentially harmful early pregnancy complications, such as ectopic pregnancy, can be ruled out. Similarly, it has also been suggested that, for certain patient groups, higher volume leads to better outcomes, possibly due to greater exposure of clinicians to complex cases, which contributes to better collective team experience and learning [5, 6].

To our knowledge, the cost-effectiveness of EPAUs or different EPAU configurations has never been investigated. The latest NICE guideline on Ectopic Pregnancy and Miscarriage (CG 154) [7] recommended research to establish how different models of care within EPAUs might impact on service outcomes, clinical outcomes, and women’s experience of care. Given the considerable variation between different units and the lack of available health economic evidence, we aimed to examine the costs, health gains and cost-effectiveness associated with different EPAU configurations. This information should assist in making evidence-based recommendations about the future configuration of EPAUs in the UK.

Methods
Data for this health economic evaluation were collected as part of the VESPA study, a UK-wide prospective mixed-methods study on “Variations in the organisation of EPAUs in the UK and their effects on clinical, Service and PAatient-centred outcomes” [8]. Following a national survey of EPAUs in the UK, units were randomly selected and invited to participate, with an aim to achieve a sample size of 44 units. The random sampling procedure was conducted to achieve an equal distribution of unit characteristics based on the stratification criteria (planned weekly consultant presence (yes/no), the number of patients seen over 1 year, as reported by the clinicians in charge (low volume of <2500 appointments annually and high volume of ≥2500) and weekend opening (yes/no)). Full details of the recruitment and random sampling procedure are described elsewhere [8].

The recruitment of the units was completed between December 2015 and April 2016. The inclusion criteria for participants were 1) pregnant women (16 years of age and over), b) attending EPAUs because of suspected early pregnancy complications. Women who were haemodynamically unstable or in severe pain were not approached to participate in the study, as they are not routinely seen in an out-patient setting, such as an EPAU. Each participating EPAU was asked to recruit a minimum of 150 consecutively presented women. A total of 6606 women were recruited to the VESPA study. Resource use data was available for 6531 patients. Of the 6606 women recruited, a total of 4217 consented to participate in the Quality of Life questionnaire arm of the study, 414 subsequently presented women. A total of 6606 women were recruited to the VESPA study. Resource use data was available for 6531 patients. Of the 6606 women recruited, a total of 4217 consented to participate in the Quality of Life questionnaire arm of the study, 414 subsequently withdrew consent, and the remaining 3803 completed the questionnaires.

Eight unique unit configurations were considered and units were divided into the following configurations:

1. Low volume, no consultant presence, no weekend opening (vcw)
2. Low volume, no consultant presence, weekend opening (vcW)
3. Low volume, consultant presence, no weekend opening (vCW)
4. Low volume, consultant presence, weekend opening (vCW)
5. High volume, no consultant presence, no weekend opening (Vcw)
6. High volume, no consultant presence, weekend opening (VcW)
7. High volume, consultant presence, no weekend opening (VCw)
8. High volume, consultant presence, weekend opening (VCW).
Costs
Data were captured on resource use relating to EPAU visits and the entire care pathway for each of the patients was analysed. Resource use during the visit(s) included staff contact time, blood tests ordered, ultrasounds conducted, and admissions for surgery or observation. All members of staff, including administrative and clinical staff, who had contact with women attending the early pregnancy service were asked to record the type of interaction, the start and end time of their interaction, as well as their staff type. This provided an exact salary cost for each patient based on the salary cost of the staff who provided care and assistance to that patient during their EPAU appointment(s) [8].

A complete case approach was used i.e. costs were only estimated if data were available for each aspect of resource use [9]. Costs were analysed adjusting for the stratification variables (consultant presence, weekend opening and volume) as well as for age and final diagnosis. We used a multi-level model to estimate adjusted costs, allowing for clustering at the unit level. Multi-level models have been recommended for use in health economics, as they are able to incorporate the hierarchical structure of data including patients within centres and provide more appropriate estimates of patient and centre-level effects than ordinary least squares models [10].

The unit cost of an ultrasound associated with an EPAU visit was estimated by the finance team at University College London Hospital as £49.21. The cost of a blood test was based on a study by Czoski-Murray et al. [11] and the cost of admissions for surgery or observation were taken from the NHS Reference Costs 2016/17 [12]. Costs were adjusted to the 2016/17 price year using the Personal Social Services Research Unit index [13]. Sources for the costs used in the primary analysis are provided in Supplementary Table 1. No discount rate was applied as all costs were incurred within 1 year.

Quality of life
Quality of life data was captured using the EQ-5D-5L questionnaire [14] before the consultation at the initial visit and again between two and 6 weeks post-discharge from the EPAU. This validated questionnaire asks patients to score their own health based on five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems and extreme problems. This selection results in a five-digit number that is converted into a number between 0 (equivalent to death) and 1 (full health) that expresses the patient’s self-reported health at each time point. The replies were then converted to an index score using the value set for England reported by Devlin et al. [15] Index scores were in-turn used to calculate Quality Adjusted Life Years (QALYs) using the area-under-the-curve approach [16].

Anxiety score data were collected using the Visual Analogue Anxiety Scale (VAS-A) [17] prior to clinical assessment for every visit; whether an initial or clinical follow-up visit. Patients also completed the same scale at the end of every visit. Patients were asked to indicate on a horizontal line (with marks going from 0 to 100) how anxious they felt at that moment, with a mark at the extreme left indicating ‘not at all anxious’ and a mark at the extreme right indicating that they were the ‘most anxious they could ever imagine’. Pre- and post-assessment scores were then compared.

Presentation of results
We calculated mean total costs per patient, by diagnosis and for each configuration. We also looked at change in QALYs and mean change in anxiety pre- and post- consultation. STATA/MP 16.0 was used for all analyses and p values ≤0.05 were deemed statistically significant. A probabilistic sensitivity analysis (PSA) was carried out, which reflects uncertainty around the estimates of costs and QALYs [18, 19]. As the probabilistic analysis requires simulated samples from the mean cost and QALY estimates, Monte Carlo simulation was performed within Excel (Microsoft Corporation, Redmond, WA, USA) to obtain 10,000 simulated samples. A gamma distribution was used for costs and a beta distribution for QALYs.

For each configuration, we analysed the expected total QALYs and expected total cost, averaged over the simulation sample, together with 95% confidence intervals (CIs). We also computed net monetary benefit (NMB) for a given willingness-to-pay per QALY, λ, (ceiling ratio) where NMB is defined as:

\[
NMB = \text{utility} \times \lambda \cdot \text{cost}
\]

This converts utilities to a monetary scale, so that the costs and QALYs can be compared directly. Expected NMB is the average net benefit over the simulation samples. For a given willingness-to-pay threshold λ, the optimal configuration is that with the highest expected NMB. We present expected NMB for λ = £20,000 in accordance with NICE guidelines [20].

Results
Costs
Of the 6531 women for whom resource use data was collected, complete data including data on a valid diagnosis was available for 6343. The mean total cost per patient
was £225 (SD = 537). This varied depending on final diagnosis with the mean total cost in patients with a normally developing pregnancy being £92, in patients with early embryonic demise £473 and in the 12 patients with molar pregnancy £1793 (Table 1).

Mean predicted total costs by annual patient volume, consultant presence during opening hours, and weekend opening are shown in Table 2. These costs were estimated by a multi-level model allowing for clustering at the unit level and adjusting for age and final diagnosis. Lower volume, no consultant presence and lack of weekend opening were associated with lower costs than their alternatives ($p$-values < 0.01).

A multi-level model was again used to adjust total cost for final diagnosis, age, yearly volume, consultant presence and hours open at the weekend with results shown in Table 3. No relationship was evident between the unit configuration variables (yearly volume, weekend opening and consultant presence) and total cost. Age and final diagnosis were the only variables showing a statistically significant relationship with total cost ($p$-value < 0.05). For every year increase in age, a roughly £3 increase in total cost is predicted, holding all other variables constant. All final diagnoses other than twin pregnancy, not pregnant, or ‘other’ were associated with higher costs of early pregnancy care than a final diagnosis of normally-developing pregnancy.

**Quality of life**

Complete baseline quality of life data were available for 3764 patients but only 573 women completed the questionnaire at both baseline and the 2–6 week follow-up time point. The median number of days between baseline

| Table 1 | Mean total cost by diagnosis ($N = 6343$) |
|---------|-----------------------------------------|
| Diagnosis | Mean cost (£) | Standard Deviation | Number of women |
| Normally developing pregnancy | 92 | 178 | 3344 |
| Twin pregnancy | 94 | 45 | 2 |
| Early intra-uterine pregnancy | 106 | 250 | 812 |
| Other | 112 | 77 | 3 |
| Complete miscarriage | 180 | 388 | 685 |
| Not pregnant | 238 | 607 | 12 |
| Inconclusive scan (Pregnancy of Unknown Location - PUL) | 275 | 621 | 149 |
| Early embryonic demise | 473 | 814 | 800 |
| Incomplete miscarriage | 694 | 952 | 293 |
| Retained products of conception | 1005 | 1177 | 123 |
| Ectopic pregnancy | 1493 | 950 | 108 |
| Molar pregnancy | 1793 | 790 | 12 |
| All women | 225 | 537 | 6531 |

| Table 2 | Mean total cost per patient by configuration ($N = 6340$) |
|---------|-----------------------------------------|
| Mean total cost | 95% Confidence Interval (£) | Number of women |
| Volume < 2500 | £212 | 210–214 | 3181 |
| Volume ≥ 2500 | £245 | 243–247 | 3159 |
| Consultant presence – No | £224 | 222–226 | 3752 |
| Consultant presence - Yes | £235 | 232–238 | 2588 |
| Weekend opening – No | £224 | 221–227 | 3079 |
| Weekend opening – Yes | £233 | 230–235 | 3261 |

| Table 3 | Regression results. Mean total cost per patient adjusted for patient characteristics and final diagnosis ($N = 6343$) |
|---------|-----------------------------------------|
| Coefficient | Standard Error | 95% Confidence Interval | $p$-value |
| Age | 2.74 | 0.97 | 0.84–4.64 | 0.005 |
| Normally developing Pregnancy | 15.90 | 18.96 | −21.27 – 53.07 | 0.40 |
| Early Embryonic Demise | 373.34 | 18.56 | 336.97–409.71 | < 0.01 |
| Incomplete Miscarriage | 597.60 | 28.78 | 541.18–654.01 | < 0.01 |
| Retained Products of Conception | 891.65 | 28.78 | 807.31–975.98 | < 0.01 |
| Molar Pregnancy | 1005 | 1177 | 1432.32–1961.13 | < 0.01 |
| Ectopic Pregnancy | 1398.97 | 45.64 | 1309.52–1488.42 | < 0.01 |
| Inconclusive Scan (PUL) | 165.68 | 39.23 | 88.80–242.57 | < 0.01 |
| Other | −2.56 | 330.24 | −5.307 – 525.63 | 0.99 |
| Twin Pregnancy | −61.68 | 134.90 | −121.90 – 406.96 | 0.29 |
| Yearly volume (> 2500) | 0.00 | 0.10 | −0.01 – 0.12 | 0.81 |
| Consultant presence (Yes) | 1.42 | 1.63 | −1.76 – 4.61 | 0.38 |
and follow-up was 26. A total of 2173 women completed the baseline questionnaire only with no follow-up recorded. The patients who completed the questionnaire at both baseline and the 2–6 week follow-up time point had a slightly higher baseline EQ-5D of 0.854 (SD 0.132) compared to a baseline score of 0.845 (SD 0.142) in the sample with no follow up. They were slightly older than the sample with no follow up with a mean age of 32.4 (95% CI 31.9–32.9) compared to 29.1 (95% CI 28.8–29.3). They were also slightly less likely to have had a diagnosis of normally developing pregnancy (324/572 (56.74%) compared to 1262/2173 (58.08%)). The range of diagnoses in both groups is shown in Table 4.

The mean score at baseline for patients with both baseline and 4-week questionnaires returned (573 women) was 0.854 (SD = 0.13) and at an average follow up of 26 days, was 0.91 (SD = 0.11). Table 5 demonstrates the similar increase in scores across diagnoses.

Table 6 shows baseline and follow-up index scores by configuration along with the mean index score, the SD of the mean values over patients, the QALY change (mean index score * (4/52 weeks)) and the number of women who completed the questionnaire at both time points in each configuration. The biggest QALY change was seen in configuration Vcw (high volume, no consultant presence, no weekend opening), although this was based on questionnaires from only 12 women, and the smallest in configuration VcW (high volume, no consultant presence, weekend opening).

### Table 4 Range of diagnoses in women with baseline and follow-up data

| Diagnosis                     | % in those with only baseline data | N<sup>a</sup> | % in those with both baseline and follow up data | N<sup>a</sup> |
|-------------------------------|-----------------------------------|---------------|------------------------------------------------|---------------|
| Early intra-uterine pregnancy | 13.16                             | 286           | 12.61                                          | 72            |
| Normally developing pregnancy | 58.08                             | 1262          | 56.74                                          | 324           |
| Early embryonic demise        | 10.12                             | 220           | 12.61                                          | 72            |
| Incomplete miscarriage        | 3.41                              | 74            | 4.73                                           | 27            |
| Retained products of conception | 1.33                              | 29            | 1.05                                           | 6             |
| Complete miscarriage          | 9.99                              | 217           | 10.86                                          | 62            |
| Ectopic pregnancy             | 1.7                               | 37            | 0.35                                           | 2             |
| Inconclusive scan (PUL)       | 1.98                              | 43            | 0.88                                           | 5             |
| Molar pregnancy               | 0.18                              | 4             | 0.18                                           | 1             |
| Other                         | 0.05                              | 1             | 0                                              | 0             |
| Not pregnant                  | 13.16                             | 286           | 0                                              | 0             |

<sup>a</sup> Number of women with diagnosis

### Table 5 Mean baseline and follow-up quality of life scores by diagnosis

| Diagnosis                     | Baseline index score | Standard Deviation | Index score at 4 weeks | Standard Deviation | N<sup>a</sup> |
|-------------------------------|----------------------|--------------------|------------------------|--------------------|---------------|
| Early intra-uterine pregnancy | 0.853                | 0.16               | 0.904                  | 0.12               | 72            |
| Normally developing pregnancy | 0.859                | 0.13               | 0.905                  | 0.11               | 324           |
| Early embryonic demise        | 0.822                | 0.14               | 0.927                  | 0.09               | 72            |
| Incomplete miscarriage        | 0.887                | 0.08               | 0.914                  | 0.08               | 27            |
| Retained products of conception | 0.829               | 0.12               | 0.869                  | 0.12               | 6             |
| Complete miscarriage          | 0.857                | 0.13               | 0.920                  | 0.09               | 62            |
| Ectopic pregnancy             | 0.930                | 0.10               | 0.930                  | 0.10               | 2             |
| Inconclusive scan (PUL)       | 0.852                | 0.06               | 0.987                  | 0.03               | 5             |
| Molar pregnancy               | 0.715                | –                  | 0.896                  | –                  | 1             |

<sup>a</sup> Number of women with diagnosis

### Percentages of people reporting problems at baseline and 4-weeks

The percentage of patients reporting each level of problem on each dimension of the EQ-5D-5L at baseline and 4-weeks was also explored. Table 7 shows that the positive change in patient’s overall health at 4-weeks was largely due to less people reporting pain/discomfort and anxiety/depression. Little change was seen in the percentages of women reporting problems with mobility, self-care or usual activities at baseline and 2 weeks (Table 8).
Cost per QALY at 4 weeks
The expected total costs and expected total QALYs at 4 weeks for each configuration are shown in Table 9, along with their 95% CIs, estimated from the probabilistic analysis. The table shows that the units with low volume, consultant presence, and no weekend opening (vCw) or low volume, consultant presence and weekend opening (vCW) had the lowest expected costs. The highest costs were found for units with high volume, consultant presence and no weekend opening (VCw). Configurations with high volume, no consultant presence and no weekend opening (VcW) had the highest expected QALY change at 4 weeks followed by units with low volume, no consultant presence and weekend opening (vcW). Configurations with high volume, no consultant presence and weekend opening (VcW) had the lowest expected QALY change. The minimal difference in expected QALYs between configuration types (0.007 between highest and lowest QALY changes) suggests that the configuration types could be assumed to be equivalent in terms of benefit offered on the EQ-5D scale. In this case a comparison between them should effectively be based on minimising total costs. In addition, the CIs show that there is a high degree of uncertainty in the QALY change estimates. The expected net benefit at a £20,000 willingness-to-pay threshold is highest for configurations with the lowest cost (vCw) (£1203) and lowest for configurations with the highest cost (VCw) (£1064).

Pre- and post-consultation anxiety
Patients were asked to report their anxiety pre- and post-consultation for every visit at the EPAU. Three thousand five hundred fifty pre- and post-consultation anxiety scores were available. Figure 1 shows that most people

Table 6 QALYs at 4 weeks by configuration (N = 573)

| Configuration | Baseline index score | Index score at 4 weeks | Mean index score | Standard Deviation | QALY change | Number of women |
|---------------|----------------------|------------------------|----------------|------------------|-------------|----------------|
| vcw           | 0.871                | 0.909                  | 0.890          | 0.09             | 0.068       | 112            |
| vcW           | 0.882                | 0.926                  | 0.904          | 0.07             | 0.070       | 58             |
| vCw           | 0.883                | 0.907                  | 0.895          | 0.11             | 0.069       | 76             |
| vCW           | 0.871                | 0.915                  | 0.893          | 0.09             | 0.069       | 52             |
| VcW           | 0.907                | 0.950                  | 0.929          | 0.09             | 0.071       | 12             |
| VcW           | 0.799                | 0.898                  | 0.849          | 0.13             | 0.065       | 113            |
| VCw           | 0.838                | 0.912                  | 0.875          | 0.09             | 0.067       | 56             |
| VCW           | 0.849                | 0.907                  | 0.878          | 0.09             | 0.068       | 94             |

a v low volume, V high volume, c no consultant presence, C consultant presence, w no weekend opening, W weekend opening

Table 7 Percentage of patients reporting each level of problem with pain/discomfort and anxiety/depression at baseline and 4 weeks

| Level       | Pain/discomfort | Anxiety/depression |
|-------------|-----------------|--------------------|
|             | Baseline (%)    | 2 weeks (%)        | Baseline (%)    | 2 weeks (%)        |
| No          | 42              | 60                 | 32              | 55                 |
| Slight      | 41              | 34                 | 34              | 32                 |
| Moderate    | 15              | 4                  | 23              | 11                 |
| Severe      | 2               | 1                  | 7               | 1                  |
| Extreme     | 0               | 0                  | 3               | 1                  |
| Reporting some problems | 58 | 40 | 68 | 46 |

Table 8 Percentage of patients reporting each level of problem with mobility, self-care and usual activities at baseline and 4 weeks (N = 573)

| Level                     | Mobility | Self-care | Usual activities |
|---------------------------|----------|-----------|------------------|
|                            | Baseline (%) | 2 weeks (%) | Baseline (%) | 2 weeks (%) | Baseline (%) | 2 weeks (%) |
| No problems               | 93       | 93        | 98              | 98        | 78           | 80           |
| Slight problems           | 5        | 6         | 2               | 1         | 17           | 16           |
| Moderate problems         | 1        | 1         | 0               | 0         | 4            | 3            |
| Severe problems           | 1        | 0         | 0               | 0         | 1            | 1            |
| Unable                    | 0        | 0         | 0               | 0         | 1            | 1            |
| Reporting some problems   | 7        | 7         | 2               | 2         | 22           | 20           |
(78%) experienced a decrease in their anxiety following their EPAU appointment.

The mean anxiety score pre- and post- consultation and the mean change in anxiety for each configuration are shown in Table 10. vCw had the biggest mean decrease in anxiety whereas vcW had the smallest, although differences were minimal.

**Discussion**

It is evident that the total cost per woman attending an EPAU with early pregnancy complications in terms of blood tests, ultrasounds, admissions and staff costs is, as expected, strongly dependent on the final diagnosis, and to a lesser degree the woman’s age. Over 60% of women recruited in this study had a diagnosis of normally developing or early intra-uterine pregnancy with a mean cost of £92 and £106 respectively. Women with higher service use costs were those experiencing miscarriage or molar pregnancy (£180 and £1793).

Mean total cost by configuration varied from £189 - £257 per patient when adjusted for age and final diagnosis. Patient selection was not based on the severity of their condition; all women who consecutively presented to the participating EPAUs were invited to participate.
in the study prior to establishing their diagnosis. On the basis of our pilot work, significant differences in patient condition across the different units were not anticipated [8]. The % or pregnancies that were ‘normal’ varied between 50.3 and 76.3% across all units, with a mean of 68.9%. The lowest average cost per patient was encountered in small volume units with consultant presence that were closed over the weekend, although, overall, there was little evidence to suggest that the differences in cost were related to consultant presence, volume of patients seen or weekend opening. The findings suggest that individual unit factors or the characteristics of women seen at different units drive increased admissions, and therefore differences in costs; however, given the limitations of the study design, it cannot be conclusively determined that unit configuration does not play a role.

Women’s overall health at 4 weeks measured on the EQ-5D-5L scale improved with the average score increasing from 0.854 at baseline to 0.91 at a mean follow up of 26 days for the 573 women who completed questionnaires at both time points. This was mainly due to the fact that considerably fewer women reported problems in their anxiety immediately following their EPAU appointment. A variation of 23 to 30 points on the anxiety scale across configuration types was found. The largest decrease in anxiety was shown in women who attended small volume units with consultant presence and no weekend opening.

A further limitation is the poor response rate observed at the four-week follow up period. Although best practice for maximising response rates was followed, obtaining the target number of observations at each time point required sending a large number of questionnaires. In addition, many questionnaires were returned late. For the four-week follow-up analysis, we used any questionnaire that was returned between two and 6 weeks post visit. While this approach is not optimal compared to a more positive response rate being achieved, we believe it

| Configrationa | Mean anxiety score pre-consultation | 95% Confidence Interval | Mean anxiety score post-consultation | 95% Confidence Interval | Mean change in anxiety pre and post consultation | 95% Confidence Interval |
|---------------|-----------------------------------|-------------------------|-------------------------------------|-------------------------|-----------------------------------------------|-------------------------|
| vCW           | 56                                 | (54–58)                 | 27                                  | (25–29)                 | −29                                           | (−32, −27)              |
| vCW           | 54                                 | (51–57)                 | 31                                  | (28–34)                 | −23                                           | (−27, −20)              |
| vCW           | 56                                 | (53–59)                 | 26                                  | (24–29)                 | −30                                           | (−33, −27)              |
| vCW           | 57                                 | (54–61)                 | 30                                  | (26–33)                 | −28                                           | (−32, −24)              |
| vCW           | 56                                 | (52–61)                 | 27                                  | (23–32)                 | −29                                           | (−34, −24)              |
| vCW           | 56                                 | (54–58)                 | 29                                  | (27–32)                 | −27                                           | (−29, −24)              |
| vCW           | 59                                 | (56–62)                 | 34                                  | (30–38)                 | −25                                           | (−28, −21)              |
| vCW           | 59                                 | (57–61)                 | 31                                  | (28–33)                 | −28                                           | (−31, −25)              |

a v low volume, V high volume, c no consultant presence, C consultant presence, w no weekend opening, W weekend opening

The probabilistic cost-effectiveness analysis showed that small volume units with consultant presence that were closed over the weekend had the highest expected net benefit (ENB) at a £20,000 willingness-to-pay threshold at 4 weeks (£1203). On the other end of the spectrum, small volume units without consultant presence that were open at the weekends had the lowest ENB (£1064). However, due to uncertainty, it is not possible from this data to conclusively recommend a particular EPAU configuration.
is more robust than using only questionnaires returned at 4 weeks. We believe our approach captures information on quality of life at a time point relevant to the follow-up time periods. It was also reassuring to find that the group that completed the questionnaire within this timeframe was representative in terms of diagnoses (the largest predictor of costs and outcomes).

Conclusions
Our study has shown that EPAU configuration, as specified in this study, had limited impact on costs, anxiety or health outcomes measured as QALYs although this may be due to issues with the configuration allocation. As we were unable to compare hospitals with an EPAU against hospitals without an EPAU, it is difficult to form a conclusion on whether EPAUs are cost-effective in general. However, overall, it is clear that care provided in the EPAU had a positive effect on women's health and emotional wellbeing with three quarters of women reporting a decrease in anxiety scores and a positive change in their overall health at 4 weeks.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12913-022-07709-9.

Additional file 1.

Acknowledgements
This national study has been realised thanks to the participation and hard work of 44 EPAUs and their supporting research staff and a large number of patients who took the time to complete the questionnaires. We would also like to thank the study steering committee: Pat Doyle (chairperson), Professor in Epidemiology, London School of Hygiene and Tropical Medicine. Cecilia Bottomley, Lead Clinician for Early Pregnancy, Chelsea and Westminster Hospital. Elizabeth Bradley, GP, Hampstead Group Practice. Hannah-Rose Douglas, Research Lead for Analytical Services, NHS England. Marjory Maclean, Consultant Obstetrician and Gynaecologist, NHS Ayshire and Arran. Brad Manktelow, Associate Statistics Professor, University of Leicester. Alex Peace-Gadsby, chairperson, The Ectopic Pregnancy Trust.

Authors’ contributions
Edna Keeney conducted the analysis and drafted the first version of the manuscript. Maria Memtsa developed the project, was the study manager during the set-up and data collection phase, assisted with the analyses, contributed to the writing of the manuscript, provided critical feedback and helped shape the research, analysis and the manuscript. Veneta Goodhart was the study manager during the data collection phase, assisted with the analyses, contributed to the writing of the manuscript, provided critical feedback and helped shape the research, analysis and the manuscript. Gareth Ambler assisted in developing the dataset which enabled statistical analyses and provided comments on the manuscript. Nazim Khan led the workforce analysis which informed the staff costs. Jeff Round developed and supervised the analysis, contributed to the writing of the manuscript, provided critical feedback and helped shape the research, analysis and the manuscript. The author(s) read and approved the final manuscript.

Funding
This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HS&DR programme or the Department of Health and Social Care.

Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All methods were carried out in accordance with relevant guidelines and regulations. The study received a favourable ethics opinion from the North West Research Ethics Committee (reference 16/NW/0587) [see the relevant named documents for the full study approved protocol, patient and staff information leaflets and consent forms, data collection forms, unit data collection forms and unit protocol forms, URL: www.journalslibrary.nihr.ac.uk/programmes/hsdr/140441/#]. Informed consent to participate in the study was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
EK reports personal fees from Novartis Pharmaceuticals UK Ltd. (London, UK), Roche Holding AG, and from Pfizer Inc. (Pfizer Inc., New York, NY, USA), outside the submitted work. JR is currently employed by the Institute of Health Economics. The Institute of Health Economics receives funding from, and collaborates with, government, academic, not-for-profit and private-sector organisations. The Institute of Health Economics does not currently receive funds for research related to the submitted work. MM, VG, DJ, GA and NK have no conflicts of interest to report.

Author details
1 Health Economics Bristol, Population Health Sciences, University of Bristol, Bristol, UK. 2 Elizabeth Garrett Anderson Institute for Women’s Health, University College London, London, London, UK. 3 Department of Statistical Science, University College London, London, UK. 4 Modelling and Analytical Systems Solutions Ltd, Edinburgh, UK. 5 Institute of Health Economics, Edmonton, Alberta, Canada. 6 Faculty of Medicine and Dentistry, Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada.

Received: 28 January 2021 Accepted: 18 February 2022
Published online: 09 March 2022

References
1. Saving Lives, Improving Mothers’ Care: Maternal, Newborn and Infant Clinical Outcome Review Programme; Available from: https://www.npeu.ox.ac.uk/downloads/files/mbrace-uk/reports/MBRACE-UK%20Maternal%20Report%202016%20%20website.pdf
2. Biggins MA, Read MD. Management of women referred to early pregnancy assessment unit: care and cost effectiveness. Br Med J. 1991;302(676):577–9.
3. Association of Early Pregnancy Units 2016 [Available from: www.aepu.org.uk
4. Foundation H. Briefing: Emergency hospital admissions in England, which may be avoidable and how? 2018 [Available from: https://www.health.org.uk/sites/default/files/Briefing_Emergency%2520admissions_web_final.pdf
5. White AL, Armstrong PAR, Thakore S. Impact of senior clinical review on patient disposition from the emergency department. Emerg Med J. 2011;27(4):262.
6. Bell D, Lambourne A, Percival F, Laverty AA, Ward DK. Consultant input in acute medical admissions and patient outcomes in hospitals in England: a multivariate analysis. PLoS One. 2013;8(4):e61476.
7. NICE. Ectopic pregnancy and miscarriage (CG 154).
8. Memtsa M, Goodhart V, Ambler G, Brocklehurst P, Keeney E, Silverio S, et al. Variations in the organisation of and outcomes from Early Pregnancy Assessment Units: the VESPA mixed-methods study. 2020;8:46.
9. Briggs A, Clark T, Wolstenholme J, Clarke P. Missing... presumed at random: cost-analysis of incomplete data. Health Econ. 2003;12(5):377–92.
10. Leyland AH, Goldstein H. Multilevel modelling of health statistics: Wiley, 2001.
11. Czoski-Murray C, Jones ML, McCabe C, Claxton K, Oluboyede Y, Roberts J, et al. What is the value of routinely testing full blood count, electrolytes and urea, and pulmonary function tests before elective surgery in patients with no apparent clinical indication and in subgroups of patients with common comorbidities: a systematic review of the clinical and cost-effective literature. Health technology assessment (Winchester, England). 2012;16(50):i.
12. Health Do. NHS reference costs 2016–2017. London: DOH; 2017.
13. PSSRU. Unit Costs of Health and Social Care. 2017:2017.
14. [Available from: https://euroq ol.org/eq-5d-instruments/eq-5d-5l-about/]
15. Devlin NJ, Shah KK, Feng Y, Mulhen rin B, van Hout B. Valuing health-related quality of life: an EQ-5D-5L value set for England. Health Econ. 2018;27(1):7–22.
16. Hunter RM, Baio G, Butt T, Morris S, Round J, Freemante le N. An educational review of the statistical issues in Analysing utility data for cost-utility analysis. Pharmacoeconomics. 2015;33(4):355–66.
17. Atk in R. Measurements of feelings using visual analogue scale. Proc R Soc Med. 1969;62:989–93.
18. Critchfield GC, Willard KE. Probabilistic analysis of decision trees using Monte Carlo simulation. Med Decis Mak. 1986;6(2):85–92.
19. Doub let P, Begg CB, Weinstein MC, Braun P, McNeil BJ. Probabilistic sensitivity analysis using Monte Carlo simulation: A practical approach. Med Decis Mak. 1985;5(2):157–77.
20. McCabe C, Claxton K, Culver AI. The NICE cost-effectiveness threshold: what it is and what that means. Pharmacoeconomics. 2008;26(9):733–44.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.