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Physical resolution of tubal ectopic pregnancy on ultrasound imaging following successful expectant management

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Article

**Title** Physical resolution of tubal ectopic pregnancy on ultrasound imaging following successful expectant management

**Running Title** Physical resolution of tubal ectopic pregnancy

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**Abstract**

**Research Question**

What is the time required for complete physical resolution of tubal ectopic pregnancies diagnosed on ultrasound imaging in women undergoing successful expectant management?

**Design**

A prospective observational cohort study of 177 women who had successful expectant management of tubal ectopic pregnancy, who attended a single Early Pregnancy Unit between January 2014 and

December 2018. All participants were monitored until their serum  $\beta$ -hCG dropped to non-pregnant levels and with two-weekly follow-up ultrasound scans until resolution of the pregnancy.

## Results

112/177 (63.8%, 95% CI 56.3-70.9) of tubal ectopic pregnancies were indiscernible on ultrasound 2 weeks after serum  $\beta$ -hCG had returned to non-pregnant levels. In 8/177 (4.5%, 95% CI 2.0-8.7) physical resolution took longer than 78 days. There was a positive correlation between biochemical and physical resolution of tubal ectopic pregnancy ( $r=0.21$ ,  $p=0.006$ ).

## Conclusions

Physical resolution of tubal ectopic pregnancy is often prolonged and is positively correlated with initial and maximum  $\beta$ -hCG levels. Our results indicate that  $\beta$ -hCG resolution cannot be used as the end-point of expectant management of tubal ectopic pregnancy, which should be considered when counselling women and planning for future pregnancies.

## Keywords

Pregnancy, Ectopic; Pregnancy, Tubal; Pregnancy Complications

## Key Message

In a significant proportion, physical resolution of tubal ectopic pregnancy takes several weeks following the return of serum  $\beta$ -hCG to non-pregnant levels. Women should be advised to delay trying for another pregnancy for three months, to avoid resolving pregnancies being misdiagnosed as new ones and to reduce the theoretical risk of recurrent ectopic, due to temporary tubal blockage by the resolving trophoblast.

**Abbreviations**

EPU Early Pregnancy Unit

hCG-MAX The maximum serum  $\beta$ -hCG level

hCG-SUB The  $\beta$ -hCG level at the first evaluation after the maximum level

hCG-TREND Daily percentage  $\beta$ -hCG change between hCG-MAX and hCG-SUB

TEP Tubal ectopic pregnancy

thCG The time expressed as the number of days taken for the serum  $\beta$ -hCG to reduce to non-pregnant levels

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tTOT The total number of days from the initial ultrasound diagnosis of tubal ectopic pregnancy to the final ultrasound examination confirming resolution

tUSS Number of days between the  $\beta$ -hCG level reducing to non-pregnant levels and the ultrasound scan that confirmed resolution of the TEP

TVUS Transvaginal ultrasound

**Introduction**

Tubal ectopic pregnancy (TEP) is the most common of ectopic gestations. Traditionally the treatment of TEP was surgical due to perceived risk of maternal morbidity and mortality associated with conservative management (Kobayashi *et al*, 1969). Advances in non-invasive diagnosis have enabled earlier diagnosis

of TEP, usually before serious complications occur, which facilitated the use of medical treatment with methotrexate (Mol et al., 2008). In addition, improved sensitivity of transvaginal ultrasound (TVUS) imaging has enabled detection of small, failing TEPs, which are often destined to resolve naturally without the need for any medical interventions (Dooley *et al.*, 2019). This has led to the introduction of expectant management, which has now been recognised as an acceptable option to manage clinically stable women diagnosed with small TEP associated with low serum  $\beta$ -hCG levels (NICE Guideline 126, 2019). Previous studies have shown that nearly a third of all women diagnosed with TEP on ultrasound imaging can be successfully managed expectantly, thus avoiding the costs, complications and side-effects of medical or surgical treatment (Mavrelos *et al.*, 2013).

We have previously investigated the serum  $\beta$ -hCG clearance times in clinically stable women diagnosed with TEP, who were managed expectantly. We demonstrated that the median time for  $\beta$ -hCG to reduce to non-pregnant levels is 18 days and that the clearance time is directly associated with the maximum and initial rate of decline of the serum  $\beta$ -hCG level (Mavrelos *et al.*, 2015). Although the decline of the serum  $\beta$ -hCG to non-pregnant levels is considered to be the end point of successful non-surgical treatment of TEP, there are reports in the literature of women with a negative pregnancy test presenting with ruptured TEP (Lonky and Sauer, 1987; Kalinski and Guss, 2002). Additionally, there are published reports of chronic TEP, with women presenting with a negative pregnancy test and found to have a persistent solid adnexal swelling on ultrasound examination (Drakopoulos *et al.*, 2014, Savelli L *et al.*, 2013). In view of this, it is likely that trophoblastic tissue will persist within the Fallopian tube for some time after all clinical and biochemical signs of pregnancy have resolved. Previous studies have investigated small cohorts of women who have been managed with methotrexate therapy, with follow up ultrasound scans until the ectopic pregnancy was no longer visible (Brown et al. 1991). Brown et al. demonstrated that in approximately 40% of cases, the ectopic pregnancy remained visible on ultrasound scan after the serum  $\beta$ -hCG had returned to non-pregnant levels; and one case took 180 days to resolve.

It is unknown; however, in what proportion of women managed non-surgically the trophoblastic tissue will remain within the Fallopian tube, how long it will take to resolve and what are the possible associated short- and long-term risks.

The aim of this study was to monitor the changes in size of TEP which were successfully managed expectantly, after the resolution of serum  $\beta$ -hCG levels. We assessed the length of time taken for full physical resolution of TEPs and recorded all complications during this follow-up period.

## Materials and Methods

This was a prospective observational cohort study performed at a single Early Pregnancy Unit (EPU) which was carried out over a 5-year period between January 2014 and December 2018. We included all women who had a positive urine pregnancy test and presented to the clinic either with suspected early pregnancy complications or with a history of previous miscarriage or ectopic pregnancy. All women were assessed clinically and underwent a TVUS using high-end equipment (Voluson E8, GE Medical Systems, Milwaukee, WI, USA). All examinations were performed either by a consultant gynaecologist experienced in early pregnancy care or by a clinical fellow working under their direct supervision. Clinical data, ultrasound images and the results of biochemical tests were stored on a dedicated clinical database (PIA Fetal Database, version 2.23; Viewpoint Bildverarbeitung GmbH, Munich, Germany) and were available for review during women's follow up visit.

The ultrasound diagnosis of a TEP was based on direct visualization of a structure with typical appearances an extrauterine pregnancy separable from the ipsilateral ovary (Dooley *et al.*, 2019). The morphological type of the TEP was classified based on the below defined characteristics:

- I. Gestational sac containing an embryo, with visible cardiac activity
- II. Gestational sac containing an embryo, with no visible cardiac activity
- III. Gestational sac containing only a yolk sac, with no visible embryo
- IV. Empty gestational sac, with no visible additional structures
- V. Solid, homogenous swelling

Surgical management was offered to women who were diagnosed with a TEP and had presented with severe pain or were found to have significant haemoperitoneum on ultrasound examination. Where ultrasound revealed either a live embryo or TEP with a mean diameter of more than 3cm, surgical management was also recommended.

Women who had no, or only mild symptoms were offered expectant management, pending the results of the serum  $\beta$ -hCG levels. Women were confirmed as eligible for expectant management if their initial serum  $\beta$ -hCG level was less than 1500IU/L. Where the level was above this, women were advised to have surgery. Medical management is not routinely offered in our unit and is usually only considered in the context of clinical trials.

Women selected for expectant management were managed on an outpatient basis. An individualised follow-up plan was made by one of the EPU consultants based on women's initial blood results and TVUS findings. They were advised to return to the clinic or the emergency department if they experienced increased abdominal pain, before their scheduled appointment. They were also advised against long distance travel and were made aware of the small risk of tubal rupture and the need for emergency surgery.

In women with  $\beta$ -hCG levels showing sustained rise on repeated measurements, surgical management was recommended. Expectant management was discontinued if women reported significant increase in their abdominal pain or if they opted for surgical management during the follow-up.

The study population included all women diagnosed with a TEP on ultrasound scan who were managed expectantly and whose  $\beta$ -hCG levels had reduced to non-pregnant levels without the need for medical intervention. The first stage of follow-up involved monitoring of the serum  $\beta$ -hCG levels at intervals of between 2 and 7 days, until they declined to non-pregnant levels ( $<20\text{IU/L}$ ) or until the urinary pregnancy test was negative. We recorded the maximum serum  $\beta$ -hCG level (hCG-MAX) during this period, the  $\beta$ -hCG level at the first evaluation after the maximum level (hCG-SUB) and calculated the daily  $\beta$ -hCG change between hCG-MAX and hCG-SUB (hCG-TREND, % change/day). The time expressed as the number of days taken for the serum  $\beta$ -hCG to reduce to non-pregnant levels (thCG), was also documented.

The second stage of the follow-up process included a TVUS two weeks after the  $\beta$ -hCG had resolved to non-pregnant levels. Women with no evidence of ectopic trophoblastic tissue on ultrasound imaging were discharged from the clinic. In those women who had evidence of persistent TEP on the initial follow-up scan, further follow up visits at two weekly intervals were arranged until a complete resolution of pregnancy was confirmed. We documented the number of days between the  $\beta$ -hCG level reducing to non-pregnant levels and the ultrasound scan that confirmed resolution of the TEP (tUSS).

The total number of days from the initial ultrasound diagnosis of TEP to the final ultrasound examination confirming resolution (tTOT) was also documented.

Statistical analysis of the data was performed using Statistical Package for Social Sciences (version 25, 2017, IBM, New-York). In order to show a mean difference of 30 days between negative pregnancy test



and complete physical resolution of pregnancy on ultrasound scan, with confidence level of 95% and 80% power, we calculated that 170 women would need to be recruited.

The number and percentage in each category were calculated for categorical variables. The mean and standard deviation were calculated for normally distributed continuous variables, with median and interquartile range calculated if not normally distributed. Analysis of variance (ANOVA) was used to compare different ultrasound morphologies at the time of diagnosis and variables found to follow a normal distribution, whilst Kruskal-Wallis test was used for non-normally distributed variables. Spearman's rank correlation was used to examine the association between the study variables and the time measurements for resolution of TEP (thCG, tUSS and tTOT). The level of significance was set at <0.05 throughout.

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The study has been registered with the Research Registry (Unique Identifying Number: 4867). Follow up with TVUS in women diagnosed with TEP who opted for conservative management until physical resolution is confirmed is a part of our standard clinical practice. In view of that we were advised that this study did not require formal ethics approval given that patient identifiable data was not accessible to anyone outside the clinical care team.

## Results

During the study period, 14944 women attended our unit with suspected early pregnancy complications. A total of 718/14944 (4.8%, 95% CI 4.5-5.2) were diagnosed with a TEP.

The flowchart of women in this study is shown in Fig. 1. A total of 206 women had successful expectant management of TEP defined by decline of  $\beta$ -hCG to non-pregnant levels. They were all invited to attend

for further follow-up TVUS to document complete physical resolution of TEP. There were 29/206 (14.1%) women who did not complete follow up: six attended for 1 or more visits, whilst 23 did not attend for any follow-up after decline of  $\beta$ -hCG to non-pregnant levels. The study population included a total of 177 women who attended the follow-up until complete physical resolution of the TEP was confirmed on TVUS.

The average age was 32.7 years (SD 5.4 years) and 120/177 (67.8%, 95% CI 60.4-74.6) women were nulliparous. Most women [165/177 (93.2%, 95% CI 88.5-96.4)] had conceived spontaneously and 22/177 (12.4%, 95% CI 8.0-18.2) had a history of a previous TEP. The mean gestational age at the time of diagnosis was 6 weeks and 2 days (SD 1 week and 3 days). 110 (62.2%, 54.6-69.3) women who were subsequently diagnosed with a TEP and managed expectantly presented with pain and bleeding, whilst 43 (24.3%, 18.2-31.3) presented with bleeding only, 15 (8.5%, 4.8-13.6) with pain only, whilst 9 (5.1%, 2.4-9.4) were asymptomatic and presented due to a previous history of ectopic pregnancy or miscarriage.

145/177 (81.9%, 95% CI 75.4-87.3) women were diagnosed with a TEP on their first scan whilst the remaining patients had an initial inconclusive TVUS and were diagnosed with an TEP on follow up examinations.

The morphological types of TEP at the first diagnostic TVUS are shown in Table I. The mean diameter of the TEP was 12.1mm (SD 4.1mm). We found evidence of haematosalpinx in 9/177 (5.1%, 95% CI 2.4-9.4) women.

The median serum  $\beta$ -hCG and progesterone levels on the initial blood tests were 198 mU/L (IQR 80-480) and 8.2 nmol/L (IQR 3.5-27.2), respectively. In 130/177 (73.4%, 95% CI 66.3-79.8) women the initial  $\beta$ -hCG level represented the maximum level, with the remaining having an increase  $\beta$ -hCG level on follow

up blood tests before later resolving. The median overall maximum  $\beta$ -hCG level was 218 mU/L (IQR 92-516).

The median thCG was 14 days (Table II). There was a significant difference between the three morphological types of TEP, with thCG being 9 days (69.2%) longer in morphological type 3 compared to type 5.

We found that 112/177 (63.3%, 95% CI 55.7-70.4) women had resolution of the TEP on the first follow-up TVUS, which was performed at median of 14 (IQR 14-15) days after the  $\beta$ -hCG had declined to non-pregnant levels. In women who continued to have a visible TEP on the first TVUS, the mean diameter had reduced by a median of 32.0% (IQR 12-56) in comparison the initial scan. The median tUSS was 15 days with no significant difference between the three morphological types of TEP (Table II). There were no cases where the TEP did not fully resolve during the period of follow up.

A Kaplan-Meier plot demonstrating the tUSS, is shown in Figure II. 90% and 95% of TEPs had resolved 57 and 78 days after the serum  $\beta$ -hCG level had declined to non-pregnant levels, respectively. There was a significant positive correlation between tUSS and thCG, but not with any other variable (Table III).

10/177 (5.6%, 95% CI 2.7-10.1) women had unscheduled attendances to the clinic after the  $\beta$ -hCG levels had resolved to non-pregnant levels and before the TEP had resolved from the TVUS; one woman attended with bleeding and nine with pelvic pain. A small unilateral haematosalpinx was found on TVUS in one woman, with a new haemorrhagic corpus luteum cyst found in another. In the remaining eight women, no cause for their symptoms was identified. None of these women required surgical treatment.

At the TVUS that confirmed complete resolution of the TEP, 5/177 (2.9%, 95% CI 0.43-5.37) women had evidence of tubal pathology: four were found to have a hydrosalpinx and one with a persistent haematosalpinx. Residual pain was reported by 4/177 (2.3%, 95% CI 0.6-5.7) women and 2/177 (1.1%,

95% CI 0.1-4.0) complained of persistent irregular bleeding. None of them required surgical intervention.

The median tTOT was 37 days (IQR 26-56) with 90% and 95% of TEP resolving 87 and 102 days after the initial diagnosis, respectively. There were no significant differences in tTOT between each morphological type of TEP (Table II). It is shown that tTOT was positively correlated with the  $\beta$ -hCG-INIT and  $\beta$ -hCG-MAX measurements and was negatively correlated with the  $\beta$ -hCG-TREND. There was no correlation with maternal age, initial progesterone levels or the initial size of the TEP (Table IV).

There was a highly significant positive relationship between  $\beta$ -hCG-INIT and tTOT ( $p < 0.001$ ), where a one unit increase in  $\beta$ -hCG-INIT on logarithmic scale was equivalent to a 41% (95% CI 21-64) increase in tTOT (Figure III).

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At the time of analysis, 90/177 (50.8%, 95% CI 43.2-58.4) women had attended our unit with their subsequent pregnancies, with 4/90 (4.4%, 95% CI 1.2-11.0) having a repeat TEP, three in the ipsilateral and one in the contralateral Fallopian tube to the initial TEP.

## Discussion

Our study has shown that in approximately two thirds of women with TEP who are managed expectantly trophoblastic tissue became non-detectable on TVUS within 14 days of the serum  $\beta$ -hCG returning to non-pregnant levels. We also found that in nearly 5% of women it took longer than three months for the physical resolution of pregnancy to be completed.

The strengths of our study were its prospective design, clearly defined diagnostic criteria and immediate access to all ultrasound and biochemical measurements which were stored on a dedicated clinical database. The study was conducted in a tertiary referral early pregnancy unit and all ultrasound examinations were either carried out or directly supervised by expert ultrasound imaging operators using top of the range equipment. All TVUS images were digitally stored and reviewed prior to each follow-up visit to ensure consistency in the diagnosis and measurements. The weakness of our study is relatively long interval between the follow-up visits, meaning there is a possibility that we would have recorded shorter resolution times if the visits had been organized on a more frequent basis. However, daily follow-up visits are too frequent to be implemented in routine practice and we decided to approach the issues of TEP resolution from a practical clinical rather than pathophysiological perspective; with a focus on investigating the longest time to resolution. There was a relatively large 14% non-compliance rate with follow up, which is another potential weakness of the study. Our EPU serves a cosmopolitan, highly mobile inner-city population which could explain this relatively high proportion of women not attending for the full follow-up visit program.

Previous studies of TEP undergoing successful expectant management reported median serum  $\beta$ -hCG clearance times to non-pregnant levels of 18 and 19 days which was longer than 14 days recorded in our study (Mavrelos *et al.*, 2015; Helmy *et al.*, 2015). The maximum median  $\beta$ -hCG readings (463IU/L and 393IU/L) and the mean sizes of TEP pregnancies (18mm and 14mm) in previous studies were higher compared to the findings in the current study ( $\beta$ -hCG 218IU/l and size 12mm). All studies showed a significant positive correlation between the maximum recorded  $\beta$ -hCG readings and its clearance time which may explain the shorter median clearance time in our current study. The smaller TEP size in our study may reflect improved quality of ultrasound diagnosis driven by technological advances and increased experience of operators, facilitating detection of smaller TEP, which may have previously been classified as pregnancies of unknown location.

There have been no previous large studies looking at the physical resolution of TEP undergoing non-surgical management. Several case series have shown that physical resolution of interstitial pregnancies managed either expectantly or with methotrexate could take more than a year to complete (Timor-Tritsch *et al.*, 1992; Poon *et al.*, 2014). However, interstitial pregnancies, even when treated expectantly, tend to be much larger, often contain live embryo and have significantly higher  $\beta$ -hCG levels compared to TEP. In women diagnosed with Caesarean scar ectopic pregnancies reported median resolution rate with expectant management was 82 days (range 37–174) (Harb *et al.*, 2018). Prolonged resolution times have also been reported in cases of cervical pregnancies (Mangino *et al.*, 2014).

Information about the length of time required for a complete physical resolution of pregnancy is pivotal for counselling of women who are considering expectant management of TEP. Women should be informed of a very small, but significant risk of complications such as intra-abdominal bleeding and tubal rupture, which may occur for some time after decline of  $\beta$ -hCG levels to non-pregnant levels. The awareness that such a risk exists should help to increase the safety of expectant management protocols and ensure that the possibility of tubal rupture is not dismissed by clinicians because of a urine pregnancy test being negative. In addition, the presence of retained, resolving trophoblastic tissue within the Fallopian tube could theoretically cause transient tubal obstruction; increasing the risk of a recurrent TEP should new conception occur before the primary TEP has resolved. In view of that women could be advised to postpone trying for another pregnancy for three months as 95% of TEPs would resolve by then. A three-month follow-up scan could be offered to those women who are keen to try for another pregnancy as soon as possible. That would identify the small proportion in whom the resolution of TEP takes longer. However, this would be only of importance to women who are trying for a spontaneous conception and to those considering ovarian stimulation or intrauterine insemination. Women undergoing in-vitro fertilization could probably start treatment before physical resolution is completed as the presence of residual non-functional trophoblastic tissue is unlikely to decrease the

chance of successful treatment. However, it would be helpful to inform fertility specialists that resolving TEP may be visible on the ultrasound scans carried out as a part of fertility treatment, to prevent offering women unnecessary interventions.

In summary, the results of our study provide women and clinicians, for the first time, with information about the length of time required for the completion of expectant management of TEP. Future work is needed to find out how in what proportion of women presenting with acute pain following decline of  $\beta$ -hCG levels to non-pregnant levels their symptoms could be attributed to residual tubal trophoblast. There is also a need to determine whether medical treatment with methotrexate could result in faster resolution of TEP compared to the expectant management.

#### **Author's Roles**

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WD was involved with the conception and design of the work, acquisition of the data, analysis and interpretation of the data and drafting of the article. DJ was involved in conception and design of the study and drafting the article. LDB and NT were involved with the acquisition and analysis of the data, revising the article critically for important intellectual content. MM and EJ were involved with the conception and design of the study and revising the article critically for important intellectual content. All authors were involved in the final approval of the version to be submitted.

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## Ethical Approval

The study has been registered with the Research Registry (Unique Identifying Number: 4867). Follow up with TVUS in women diagnosed with TEP who opted for conservative management until physical resolution is confirmed is a part of our standard clinical practice. In view of that we were advised that this study did not require formal ethics approval given that patient identifiable data was not accessible to anyone outside the clinical care team.

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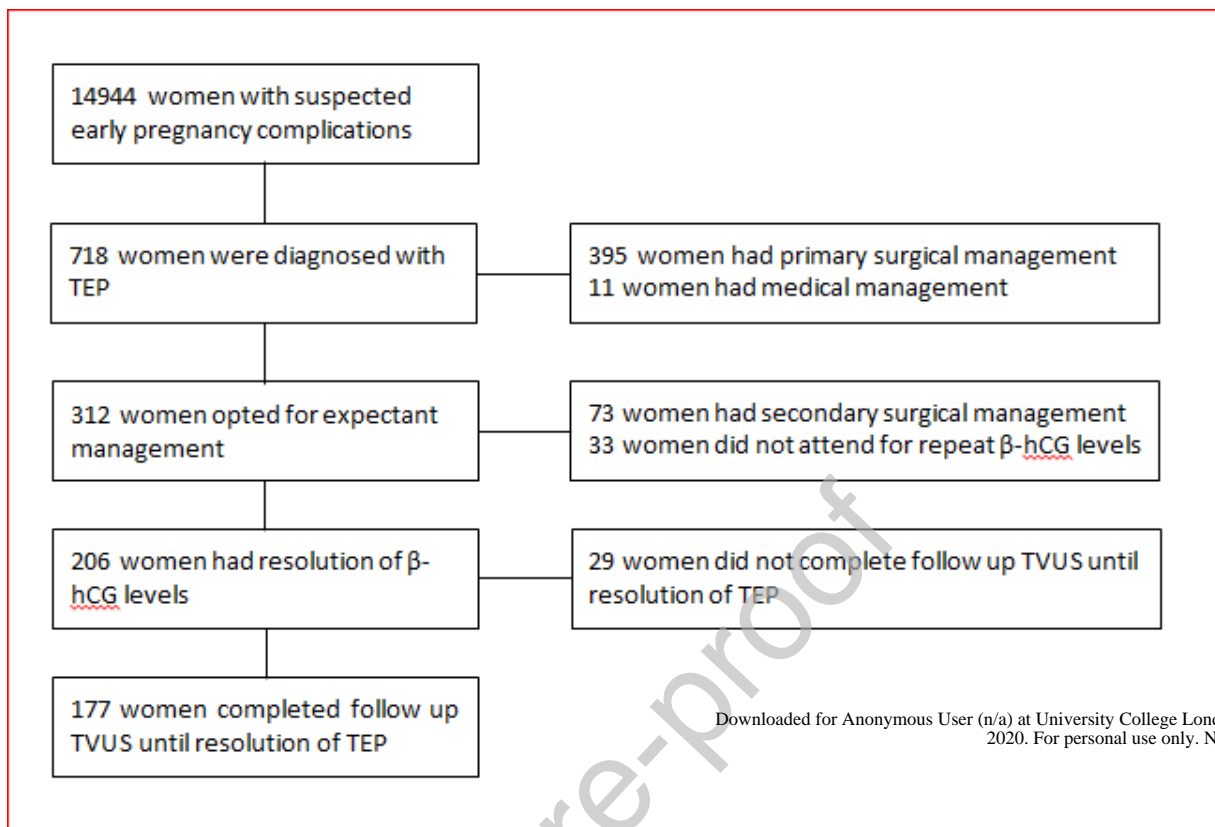
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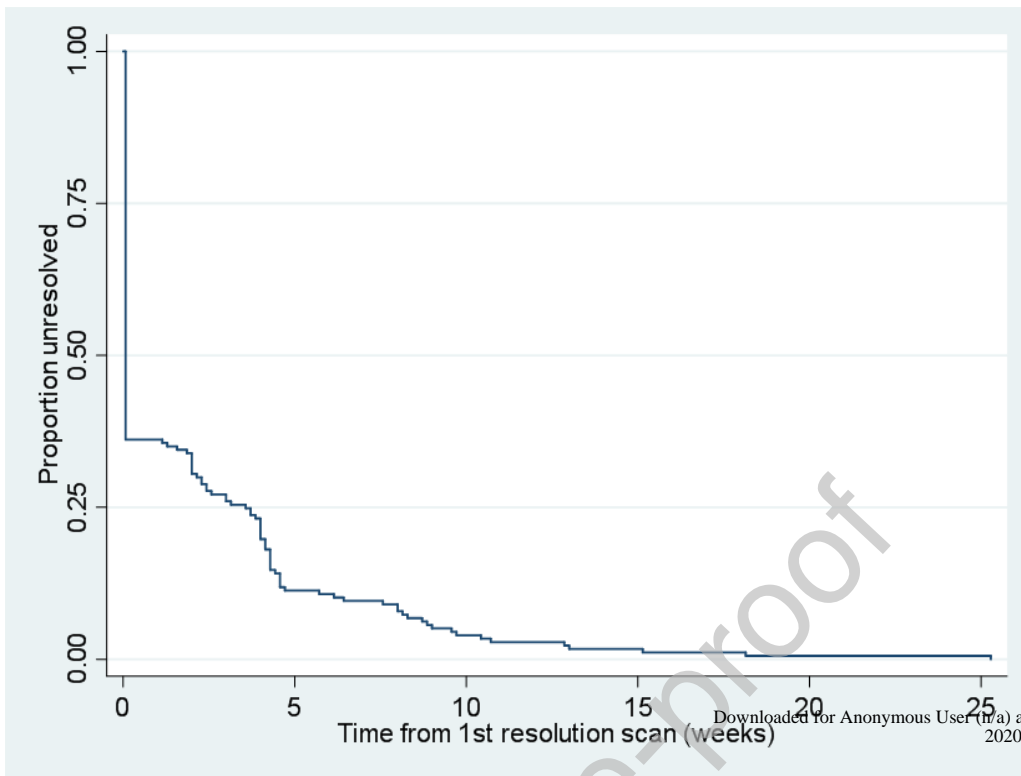
### Key Message

A complete physical resolution of tubal ectopic pregnancies managed expectantly is achieved within 78 days following the return of  $\beta$ -hCG to non-pregnant levels in 95% of women. This information will help to improve safety of expectant management of ectopic pregnancies and improve counselling of women who are planning further pregnancies.

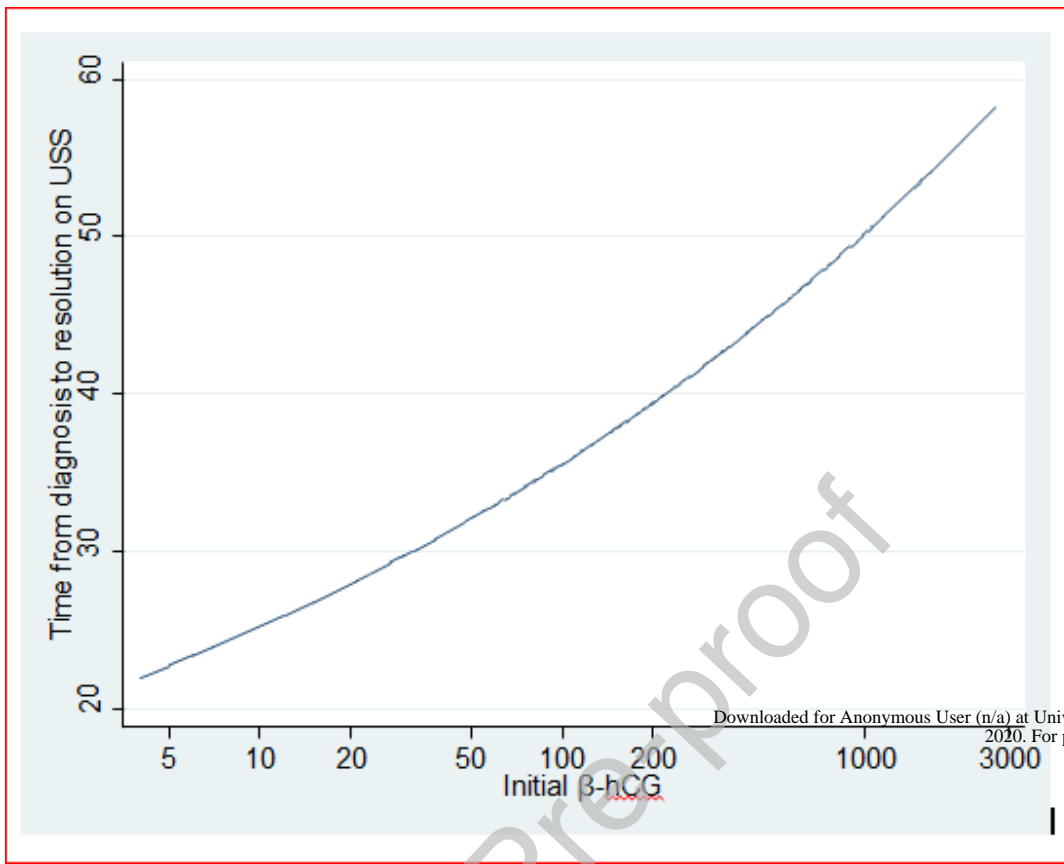


**Figure 1** Flowchart of participants through the study.

TEP, tubal ectopic pregnancy; TVUS, transvaginal ultrasound scan



**Figure II** Kaplan-Meier plot showing the number of days between the  $\beta$ -hCG level reducing to non-pregnant levels and the scan that confirmed resolution of the TEP (tUSS) (n=177).



**Figure III** A graphical illustration between the  $\beta$ -hCG-INIT and tTOT on a logarithmic scale. A statistically significant association is demonstrated between the two variables ( $p < 0.001$ ).

$\beta$ -hCG-INIT, first  $\beta$ -hCG measurement at time of diagnosis of tubal ectopic pregnancy; tTOT, total number of days from the ultrasound diagnosis of tubal ectopic pregnancy to the ultrasound scan confirming resolution

**Table I** Ultrasound morphological type at time of diagnosis of TEP for cases managed expectantly.

(n=177)

Morphological type	n (% , 95% CI)
Type 5	107 (60.5, 52.8-67.7)
Type 4	57 (32.2, 25.4-39.6)
Type 3	13 (7.3, 4.0-12.2)

TEP, tubal ectopic pregnancy

**Table II** tUSS and tTOT for all participants and a comparison between the different morphological types of TEP (n=177)

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	All patients (n=177)	Type 5 (n=107)	Type 4 (n=57)	Type 3 (n=13)	P-value
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	
thCG	14 (10, 22)	13 (10, 18)	16 (11, 26)	22 (19, 28)	0.004
tUSS	15 (14, 39)	15 (14, 37)	16 (14, 36)	18 (14, 67)	0.48
tTOT	37 (26, 56)	34 (25, 51)	40 (28, 57)	46 (36, 91)	0.12

tUSS, number of days between the  $\beta$ -hCG level reducing to non-pregnant levels and the scan that confirmed resolution of the TEP; tTOT, total number of days from the ultrasound diagnosis of TEP to the ultrasound scan confirming its resolution; TEP, tubal ectopic pregnancy; IQR, Interquartile range

**Table III** Associations between tUSS and other study variables (n=177)

	Correlation coefficient	p-value
Maternal age	0.04	0.56
Gestational age	-0.13	0.11
First $\beta$ -hCG measurement	0.14	0.07
First progesterone measurement	-0.03	0.68
$\beta$ -hCG-MAX	0.12	0.10
$\beta$ -hCG-TREND	-0.13	0.10
thCG	0.21	<b>0.006</b>
Mean diameter of TEP (at initial diagnosis)	0.11	0.15

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tUSS, the number of days taken from the  $\beta$ -hCG declining to non-pregnant levels and the physical resolution of TEP on follow up ultrasound scan;  $\beta$ -hCG-MAX, maximum serum  $\beta$ -hCG level during the period of follow up;  $\beta$ -hCG-TREND, daily % change between  $\beta$ -hCG-MAX and the first determination after this level; thCG, number of days taken for the serum  $\beta$ -hCG to reduce to non-pregnant levels; TEP, tubal ectopic pregnancy

**Table IV** Associations between tTOT and other study variables (n=177)

	Correlation coefficient	p-value
Maternal age	0.08	0.28



$\beta$ -hCG-INIT	0.31	<b>&lt;0.001</b>
First progesterone measurement	0.08	0.29
$\beta$ -hCG-MAX	0.32	<b>&lt;0.001</b>
$\beta$ -hCG-TREND	-0.32	<b>&lt;0.001</b>
thCG	0.62	<b>&lt;0.001</b>
Mean TEP width at diagnosis	0.10	0.17

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tTOT, total number of days from the ultrasound diagnosis of TEP to the ultrasound scan confirming resolution;  $\beta$ -hCG-INIT, First  $\beta$ -hCG measurement;  $\beta$ -hCG-MAX, maximum serum  $\beta$ -hCG level during the period of follow up;  $\beta$ -hCG-TREND, daily % change between  $\beta$ -hCG-MAX and the first determination after this level; thCG, number of days taken for the serum  $\beta$ -hCG to reduce to non-pregnant levels; TEP, tubal ectopic pregnancy