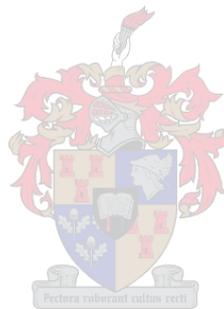


Is an educational intervention effective in improving the diagnosis and management of Suspected Ectopic Pregnancy in a tertiary referral hospital in South Africa?

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Declaration

By submitting this dissertation electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the owner of the copyright thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Dr P Wipplinger

Date: March 2010

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ABSTRACT

Study objective: To investigate whether an educational intervention in the Gynaecology Department of Tygerberg Hospital (TBH) was effective in improving the accuracy of the diagnosis and appropriateness of treatment options offered to women with suspected Ectopic Pregnancy (EP).

Methods: A retrospective cross-sectional before-and-after study was performed, including 335 consecutive patients with suspected EP before (1/3 - 30/6/2008) and after (1/9 - 31/12/2008) "the intervention". From the gynaecological admissions register all pregnant patients with symptoms potentially compatible with EP were selected and these were cross referenced with beta-hCG requests, entries in the theatre register for surgery for possible EP and methotrexate prescriptions for EP in these time periods.

"The intervention" consisted of a formal lecture presented to the registrars and consultants regarding the latest evidence-based guidelines concerning the diagnosis and management of EP. An algorithm based on this information was introduced in the emergency unit and ultrasound unit together with a prescribed ultrasound reporting form containing all the pertinent information required to follow the algorithm. Clinical decisions were left to the registrar and consultant on duty.

Primary outcomes: Time from presentation to treatment, number and appropriateness of special investigations, surgical procedures or medical management.

Secondary outcomes: Number of in-patient days and visits, adherence to the algorithm.

Results: There was a non-significant trend towards improved reporting of the uterine content and significantly less reports of definite signs of an intrauterine pregnancy (IUP) ($p < 0.001$, RR 0.46, 95% CI 0.31-0.70) due to stricter ultrasound criteria being followed. There was a significant change in the spectrum of uterine findings ($p = 0.001$), the spectrum of adnexal findings ($p = 0.006$) and the spectrum of free fluid noted ($p = 0.05$).

There was a reduction in the total number of beta-hCG levels requested at presentation (patients with no beta-hCG: 24 vs 34, $p = 0.05$, RR 1.60, 95% CI 0.99-2.59) with a significant reduction in the number of inappropriate beta-hCG requests (77 vs 40, $p < 0.001$, RR 0.60, 95% CI 0.43-0.81). There was a significant difference in the spread of the number of beta-hCG tests per patient with less repeat tests in the study group ($p = 0.021$).

Significantly less manual vacuum aspirations (MVAs) were performed (47 vs 21, $p = 0.003$, RR 0.51, 95% CI 0.32-0.81) but there was no change in the other treatment modalities offered nor in the time from presentation to treatment, number of visits or in-patient days. Adherence to the algorithm was poor (59 %).

Conclusions: Except for a significant decrease in the MVAs performed, with possibly less interrupted early intrauterine pregnancies, the improvement in the use of special investigations after "the intervention" did not translate into fewer inappropriate diagnoses and management. This could be due to frequent non-adherence to the algorithm, and widespread implementation of the algorithm as well as continuous audits would be necessary before a future study could be attempted to assess the efficacy of the algorithm.

Is 'n opvoedkundige intervensie effektief in die verbetering van die diagnose en hantering van vermoedelike ektopiese swangerskappe in 'n tersiêre verwysingshospitaal in Suid-Afrika?

OPSOMMING

Studiedoelwit: Die hoofdoel van hierdie studie is om te ondersoek of 'n opvoedkundige intervensie in die Ginekologiese afdeling van Tygerberg Hospitaal (TBH) doeltreffend sou wees in die verbetering van die akkuraatheid van diagnose en die gepastheid van behandelingsopsies wat aan vroue gebied word met 'n vermoedelike ektopiese swangerskap (ES).

Metodes: 'n Retrospektiewe, kruisdeursnee voor-en-na studie rakende 335 opeenvolgende pasiënte wat 'n vermoedelike ES het voor (1/3/2008 – 30/6/2008) en na (1/9/2008 – 31/12/2008) "die intervensie". Swanger pasiënte is uit die ginekologiese toelatingsregister geselekteer indien hulle simptome gehad het wat moontlik verbind kon word met ES. Hulle is kruisverwys met die beta-hCG's aangevra, inskrywings in die teaterregister vir chirurgie vir moontlike ES en ginekologie-pasiënte wat metotrexate vir ES binne hierdie tydperke ontvang het.

"Die intervensie" het bestaan uit 'n formele lesing aan die kliniese assistente en konsultante ten opsigte van die jongste bewysgebaseerde riglyne rakende die diagnose en hantering van ES. 'n Algoritme gegrond op hierdie inligting is in die noodeenheid en ultraklank-afdeling ten toon gestel asook 'n voorgeskrewe ultraklank rapporteringsvorm met al die toepaslike inligting wat vereis word om die algoritme te volg. Kliniese besluite is aan die kliniese assistent en konsultant aan diens oorgelaat.

Primêre uitkomst: Tydsduur vanaf aanmelding tot behandeling, aantal en gepastheid van spesiale ondersoeke, chirurgiese prosedures en mediese hantering.

Sekondêre uitkomst: Die aantal binnepasiëntdae en besoeke, nakoming van die algoritme.

Resultate: Daar was 'n nie-betekenisvolle neiging tot beter rapportering van die uteriene-inhoud en betekenisvol minder rapportering van definitiewe tekens van 'n intra-uteriene swangerskap (IUS) ($p < 0.001$, RR 0.46, 95% CI 0.31-0.70) as gevolg van strengere ultraklankstandaarde gevolg. Daar was 'n betekenisvolle verandering in die spektrum van uteriene bevindinge ($p = 0.001$), die spektrum van die adneksale bevindinge ($p = 0.006$) en die spektrum van die vrye vog aangeteken ($p = 0.05$).

Daar was 'n vermindering in die totale aantal beta-hCG-vlakke aangevra met aanmelding (pasiënte met geen hCG: 24 vs 34, $p = 0.05$, RR 1.60, 95% CI 0.99-2.59) met 'n betekenisvolle vermindering in die aantal onvanpaste beta-hCGs aangevra (77 vs 40, $p < 0.001$, RR 0.60, 95% CI 0.43-0.81). Daar was 'n betekenisvolle verskil in die verspreiding van die aantal beta-hCG-toetse per pasiënt, met minder herhalende toetse in die studiegroep ($p = 0.021$).

Betekenisvol minder manuele vakuüm aspirasies (MVAs) is uitgevoer (47 vs 21, $p = 0.003$, RR 0.51, 95% CI 0.32-0.81), maar geen verskil in ander behandelingsmodaliteite is aangebied nie, asook geen verskil in die tydsduur vanaf aanmelding, die aantal besoeke of die aantal binnepasiëntdae nie. Nakoming van die algoritme was swak (59%).

Gevolgtrekkings: Behalwe vir 'n betekenisvolle afname in die MVAs uitgevoer, met

moontlik minder onderbroke vroeë IUS, het die verbetering in die gebruik van spesiale ondersoeke ná “die intervensie” nie minder onvanpaste diagnoses en hantering tot gevolg gehad nie. Dit kan die gevolg wees van gereelde nie-nakoming van die algoritme, en uitgebreide implementering van die algoritme asook voortdurende oudits sal nodig wees voor ‘n verdere studie aangepak kan word om die doeltreffendheid van die algoritme te bepaal.

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Introduction

1. Significance of Ectopic Pregnancy (EP)

EP remains a major cause of maternal morbidity and mortality and pregnancy losses. Confidential enquiries into maternal deaths in South Africa (CEMD, 2002-2004) have identified EP as the primary obstetric cause of death in 1.4% of all maternal deaths. Avoidable factors are often (63%) identified in cases of maternal deaths⁽¹⁾. EP also represents major health care costs⁽²⁾ and places a significant burden on emergency medical services. EP may also lead to long-term consequences including compromised future fertility.⁽³⁾ Recent studies show that the incidence of EP is increasing worldwide^(4,5), but fortunately maternal morbidity and mortality due to EP can be reduced significantly with the use of a trans-vaginal ultrasound (TVUS) where available.⁽⁶⁾

2. Benefits of early diagnosis of EP

EP can mimic many other conditions and any woman of childbearing age with abdominal pain, vaginal bleeding, or amenorrhoea with risk factors should receive a urinary pregnancy test (98-100% sensitivity) to ensure early detection of a pregnancy and consideration of EP in the differential diagnosis.⁽⁷⁾ Early diagnosis of EP changes the presentation from a life-threatening disease needing emergency open surgery to a more benign condition with other treatment options (including minimal invasive surgery (laparoscopic) or medical therapy).⁽⁸⁾

Already in 1997 Mascarenhas et al stated that laparoscopic or medical treatment should replace laparotomy in the treatment of EP.⁽⁷⁾ In 1993, Ankum voiced the opinion that a laparoscopy should be the treatment of EP and no longer be used as a diagnostic modality.^(9,10) Laparoscopic surgery for EP is safe and effective and has been shown to produce outcomes equivalent to those of laparotomy with lower costs, shorter hospital stays and quicker return to normal activity.^(11,12) Surgery can be avoided altogether for women with an early diagnosed unruptured EP: in 17 studies, 400 patients were treated with IM methotrexate (MTX) (50mg/m²) with an overall success rate of 92% (95% confidence interval of 89% to 95%).⁽¹¹⁾ MTX was cost effective⁽¹³⁾ with a low incidence of side-effects.⁽¹¹⁾

3. Difficulty of diagnosing EP

A clinical diagnosis of EP remains difficult as EP can present with widely varying clinical features ranging from no signs or symptoms at all to class 4 shock with signs of an acute abdomen.⁽¹⁴⁾ An accurate diagnosis therefore often relies on pelvic ultrasound findings but these can range from no abnormal features at all to free fluid in the peritoneal cavity, the presence of an adnexal mass, an atypical fluid collection in the uterus or a viable gestation outside the uterine cavity.^(15,16,17) With the exception of the latter none of these features are pathognomonic, lacking both sensitivity and specificity since they can also be found in the presence of an intact early intrauterine pregnancy (IUP).⁽¹⁸⁾

In the clinically stable patient, inconclusive findings are often followed by additional special investigations (including beta-hCG levels) and repeat TVUS in order to reach a more conclusive diagnosis before initiating treatment. However when this is not done in a logical and systematic manner, it may lead to unnecessary expenses, a delay in diagnosis and increased morbidity. Various algorithms have been described in an attempt to assist in the

diagnostic work up.

4. Benefits of diagnostic algorithms

It has been widely accepted that algorithms in combination with increased awareness and knowledge of risk factors among clinicians and patients, enable early and accurate diagnosis of EP.⁽⁸⁾

a. Algorithms that show the accuracy of the diagnosis

In a prospective study, Ankum 1993 et al showed their algorithm, using TVUS in combination with beta-hCG, to have a sensitivity of 0.97, a specificity of 0.95, a positive likelihood ratio of 19.4 and a negative likelihood ratio of 0.03.⁽⁹⁾ The algorithm thus proved reliable in the safe management of patients at risk for EP, and rendered laparoscopy obsolete as a diagnostic tool.^(9,10)

In a prospective study, Barnhart (1994) demonstrated a 100% sensitivity and 99,9% specificity in diagnosing EP with another diagnostic algorithm combining quantitative beta-hCG and TVUS.⁽¹⁹⁾

Mol (1998) et al suggested that repeat beta-hCG levels render more comprehensive diagnostic information than a single absolute beta-hCG value. He also emphasised that certain TVUS abnormalities carry more weight in diagnosing EP than others, and that this should be taken into account when interpreting beta-hCG levels. A patient with an ectopic mass or free fluid in the pouch of Douglas for example may need a cut-off value of only 1500 IU/L to consider EP, whereas no abnormalities on TVUS suggests a cut-off of 2000 IU/L.⁽²⁰⁾

Furthermore, Gracia et al compared six published algorithms of diagnosing EP, and found that using TVUS as the first step in diagnosis, combined with quantitative beta-hCG as indicated, was the most efficient and accurate method. No EPs were missed, few potential intrauterine pregnancies were interrupted inadvertently and diagnoses were achieved timeously.⁽²¹⁾

b. Algorithm studies that show an improvement in outcome parameters

A retrospective study by Mertz et al in 2001 showed that a diagnostic algorithm was superior to individualised evaluation in reducing the occurrence of tubal rupture.⁽²²⁾

Stovall and Ling (1993) combined history taking, physical examination, quantitative beta-hCG levels, serum progesterone, colour-flow vaginal doppler sonography and endometrial curettage in a diagnostic algorithm and expectant, medical and surgical management in a treatment algorithm. They concluded that the “rapid-yet-accurate” diagnosis of EP based on their algorithm resulted in fewer ruptured EP, virtually eliminating diagnostic laparoscopy and culdocentesis and increasing the use of MTX and expectant management of EP.⁽²³⁾

There is thus little doubt that algorithms, in a research setting, have great potential to improve diagnosis, management and outcome of EP. However, the question is not answered in terms of what the impact would be of their introduction in a busy clinical

setting with a patient profile that may differ significantly from the reported studies. Of particular note is the lack of any data on the use of algorithms for EP in developing countries.

Although many studies have supported the use of algorithms, it is necessary to validate such algorithms for one's own patients and in the local medical set-up.⁽²⁴⁾

5. Motivation to undertake the study at Tygerberg Hospital (TBH)

EP represents a major portion of the workload in gynaecological emergencies in TBH. In 2007, laparotomy for suspected or confirmed EP was the most commonly performed gynaecological procedure in the Obstetrics & Gynaecology (O&G) department and the majority of these procedures were done as emergencies and after hours. To date, it has never been investigated whether this is due to late presentation by patients or ineffective healthcare delivery. It has also never been evaluated whether other (less costly and less time-consuming) treatment options would have been appropriate for these patients. Anecdotal cases of unnecessary delays in diagnosis leading to tubal rupture, inappropriate use and unnecessary repeated use of special investigations, the occurrence of negative laparotomies and inadvertent interruptions of intact early IUPs have raised further concern about suboptimal management of this common and serious condition. These concerns formed the motivation for this study, to document the current diagnostic workup and treatment of patients with suspected EP in the O&G department at TBH and to assess whether their outcome was improved by introducing a more systematic and evidence-based approach.

The main aim of this study was to investigate whether an educational intervention and the introduction of a diagnostic and management algorithm for suspected EP in the busy O&G department of TBH have been effective in improving the accuracy of diagnosis and appropriateness of treatment options offered to women with suspected EP.

Methods

Type of study: Retrospective cross-sectional before-and-after study.

Research population: Women of reproductive age from the surrounding drainage area, primarily presenting or being referred to the emergency gynaecological unit at TBH. The population represents mainly women of low socio-economic status in the urban area of the Cape Town Metro East region, predominantly of mixed descent or African ancestry.

Study group: Women were selected retrospectively from the entries in the gynaecological emergency register if they were pregnant with symptoms suggestive of EP (e.g. lower abdominal pain and/or vaginal bleeding), if they were referred from primary care for possible EP or if they had ultrasound findings highly suggestive of EP in spite of being asymptomatic. Patients with an obvious active miscarriage or a live embryo in the uterine cavity *at presentation* were excluded from this cohort. To ensure that no suitable patients were missed, the cohort was cross referenced with all gynaecology ward admissions with a diagnosis of possible EP, all beta-hCGs requested from the gynaecology emergency unit or outpatient clinic, all entries in the theatre register for surgery for possible EP and all gynaecology patients who received MTX.

The study included all consecutive patients over four months before (1/3 – 30/6/2008) and four months after (1/9 – 31/12/2008) the “intervention”.

The intervention: A formal lecture given on 7/8/2008 to all gynaecology registrars (compulsory) and consultants (voluntarily) in the department of O&G at TBH as part of the weekly academic programme. The lecture included detailed information on evidence-based diagnostic and management options concerning EP, and an algorithm (Addendum A) based on the evidence presented was introduced. After the lecture, the algorithm was made available in poster format in the emergency O&G admission area and ultrasound unit to ensure easy access and reference. Registrars were encouraged to make use of the algorithm both for diagnosis and treatment, but the final clinical decisions were left to the clinical team (i.e. registrar and consultant on duty). At the same time a structured report format for all early pregnancy TVUS (Addendum B) was introduced to ensure that all necessary information was obtained to allow following the algorithm.

Information was gathered retrospectively from the medical records by one researcher (WP) in the form of a datasheet. Information was obtained on the dates of initial presentation, further visits, start of treatment and discharge, the patient’s condition at presentation and at initiation of treatment (stable or unstable), EP’s condition at presentation and at treatment (unruptured or ruptured), the number of special investigations (ultrasound and beta-hCG) and their results, the final diagnosis, adherence to the algorithm, the final treatment and outcome.

Primary and secondary objectives were extrapolated from this.

The primary outcomes examined were:

1. Time from presentation to diagnosis
2. Special investigations (appropriate and inappropriate) prior to final treatment.
3. Number of surgical procedures (type, appropriate and inappropriate) (during/after hours) or medical treatment. Treatment was seen as appropriate if done in accordance with criteria set out in the algorithm. Unsafe MVAs were considered as MVAs not done in accordance with the algorithm and being either unnecessary or possibly interrupting a viable IUP.

Secondary outcomes were:

1. Number of visits
2. Number of in-patient days
3. Adherence to the algorithm

Each case was evaluated by two researchers (WP and GL), and while giving the clinical team the benefit of the doubt, special investigations (ultrasound and beta-hCG) and visits that did not contribute to a timely and accurate diagnosis (as suggested by the algorithm) were documented as unnecessary. Inappropriate management included surgery done when medical management should have been offered, a negative laparotomy that could have been avoided, MVA performed when an early IUP should have been considered and medical management offered to patients who did not qualify for MTX as defined by the algorithm. Follow-up appointments that did not contribute to a timely and accurate diagnosis (in accordance to the algorithm) and discharge of patients before an accurate diagnosis was made was also documented as inappropriate.

After the data collection was completed for the study, a questionnaire aimed at exploring registrars' views on the EP algorithm and gynaecological ultrasound reporting form (Addendum C) was completed by the registrars working in the gynaecological department

during the time of the study period (after the intervention).

Data Management and Statistical Analysis

Since the background incidences of the outcome variables (for example inappropriate management) are entirely unknown, the assumption was made that there would be 40% of the control group with a primary outcome of inappropriate special investigations, which would serve as a surrogate marker for inappropriate management. In order to demonstrate a 50% reduction in the rate of inappropriate special investigations requested (i.e. from 40% in the control group to 20% in the study group), a sample size of 188 patients was required (94 in each arm). The sample size was calculated using the power of 80 with a confidence level of 95%.⁽²⁷⁾

Data from the datasheets was anonymised and transferred to Excel in spreadsheet format. SPSS statistical package (version 17.0) was used for data-analysis. Normally distributed data was compared by students' t-test or Fisher's exact test where numbers were small. Non-parametric data was compared by Chi-square test or Mann Whitney-U test. $P < 0.05$ was considered as statistically significant. The relative risk with 95% confidence intervals was documented only if there was a statistical significant difference between the control and the study patients.

Results

We identified 335 patients according to the method mentioned: 178 in the period before “the intervention” (controls) and 157 in the period after “the intervention” (study patients). Base-line demographic and clinical characteristics of the study population are demonstrated in Table 1 and shows no significant difference between the two groups.

Table 1: Demographic and background characteristics of the control and study patients

Characteristics	Controls (Before intervention) n=178	Study patients (After intervention) n=157	p-values
Age [~]	28.4 ± 6.6	28.4 ± 6.7	0.4
Gravidity [^]	2 (1-11)	2 (1-8)	0.8
Parity [^]	1 (0-7)	1 (0-5)	0.6
Previous T ₁ miscarriage [#]	42	31	0.3
Previous T ₂ miscarriage [#]	2	2	0.6
Previous EP ^{#, ♪}	8	8	0.6
Previous tubal surgery [#]	10	2	0.6
Previous Infertility ^{#, *}	10	10	0.8
Amenorrhoea (weeks) [~]	8.9 ± 16.6	9.2 ± 17.8	0.4
Duration not recorded [#]	33	19	

n: Number; #: Data in number of patients (n), ~: mean ± standard deviation; ^: median (range).

♪ 1 missing data; * 2 missing data; T1: first trimester; T2: second trimester; EP: ectopic pregnancies

Clinical characteristics of the population at presentation were compared between control and study patients in Table 2. Fewer study patients had an ultrasound examination (p=0.008, RR 0.30, 95% CI 0.11-0.78) or pregnancy test (p=0.005, RR 0.46, 95% CI 0.26-0.81) prior to presentation.

Table 2: Comparison of clinical characteristics at presentation between the control and study patients

Characteristics	Controls (n=178)	Study patients (n=157)	p-value	RR – 95% CI
Presenting Symptoms				
Amenorrhoea [†]	36	35	0.6	
Vaginal Bleeding [†]	130	119	0.5	
Pain [†]	133	113	0.6	
No Pain + No Vaginal Bleeding	8	8	0.8	
Prior ultrasound	19	5	0.008	0.30 (0.11-0.78)
Prior pregnancy test	37	15	0.005	0.46 (0.26-0.81)
HCG at presentation [*]	8 669.5 ± 17 007.1	7 624.4 ± 16 124.7	0.6	
Unstable at presentation	20/178	22/157	0.4	
Unstable at final treatment [*]	22/168	22/146	0.6	

n: number of patients;

† 3 missing data; ♣ mean HCG in mIU/ml ± standard deviation; * 21 patients were lost to follow-up.

RR (95% CI): Relative Risk with 95% Confidence Intervals

Of the 335 patients, 293 were stable up until their first presentation to TBH, but 21 of these patients were lost to follow-up. Two of the 293 patients (both in the control group) became unstable prior to treatment.

The first patient (case 1) presented with pain and vaginal bleeding with a history of six weeks amenorrhoea. She had no prior pregnancy tests or ultrasonography, and a formal ultrasound scan showed an empty uterus with a 26x22x24mm adnexal mass, no fetal pole and a moderate amount of free fluid. A subsequent beta-hCG was 4762 mIU/ml and the attending doctor decided on medical management because the patient was stable and had mild pain only with no peritonism. The patient was admitted due to transport issues, and 10 hours after a first dose of MTX was administered she complained of increased abdominal pain and became unstable, whereupon she was taken to theatre and had a laparotomy and left salpingectomy for a ruptured EP with “3+” haemoperitoneum.

The second patient (case 2) presented with pain, vaginal bleeding and six weeks amenorrhoea. Only an informal ultrasound was done as she presented on a Sunday, with findings of a decidual reaction of 31mm in the uterus, a gestational sac (GS) of 15mm, no fetal pole seen and minimal free fluid in the pouch of Douglas. The diagnosis was documented as an early IUP and the plan was to admit the patient for observation and request a beta-hCG. Six hours later the patient collapsed and was found to be unstable with an acute abdomen. At emergency laparotomy, a ruptured right tubal EP was found with two litres of blood in the abdomen. The beta-hCG was not available during the diagnostic assessment with ultrasound and later documented as 5839 mIU/ml.

Data on the management of patients in both groups is presented in Table 3. There were no differences in outpatient visits, admissions or blood transfusions.

Table 3: Comparison of management between the control and study patients

Management	Controls n=178	Study patients n=157	p-value
Visits			
Patients with one visit	107	94	1.0
Total Necessary visits	256	231	0.8
Total Unnecessary visits	19	19	0.8
Admissions			
Inpatient days/patient*	0 (0-10)	2 (0-8)	0.3
Total admitted patients	88	87	0.3
Blood transfusion			
Units of blood/patient*	0 (0-6)	0 (0-8)	0.7
Patients receiving blood	26	27	0.7

n=number of patients
****Median (Range)***

Table 4 presents data on the performance and results of informal and formal ultrasound examinations.

All ultrasound examinations were performed transvaginally and classified as *informal* when done by registrars, and *formal* when done by trained sonologists in the ultrasound department at TBH.

Table 4: Results of ultrasound examinations of the control and study patients

Ultrasound	Controls n=178	Study patients n=157	p-value	RR (95% CI)
Patients who received an ultrasound examination	174	149	0.2	
<i>Total ultrasound</i>	265	252		
Ultrasound per patient*	1 (0-4)	1 (0-5)	0.3	
Necessary Ultrasound				
Ultrasound per patient*	1 (0-4)	1 (0-4)	0.4	
Total patients	174	149	0.2	
Total ultrasound	262	240		
Unnecessary Ultrasound				
Ultrasound per patient*	0 (0-1)	0 (0-2)	0.045	
Total patients	3	9	0.05	3.40 (0.94-12.34)
Total ultrasound	3	12		
Informal Ultrasound				
Number of patients	164	142	0.6	
Uterine content not noted	22	11	0.1	0.1
Gestational sac	42	18	0.01	0.50 (0.30-0.82)
Fetal pole not noted	7	2	0.6	
Fetal pole present	15	3	0.1	
Fetal pole not present	7	6	0.15	
Too early for fetal pole	13	7	0.6	
Fetal heart not noted	7	2	0.4	
Retained products	18	6	0.03	0.39 (0.16-0.94)
Adnexal appearance not noted	69	30	< 0.001	0.50 (0.35-0.72)
Free fluid				
Presence not noted	81	46	0.003	0.66 (0.50-0.87)
Amount not noted	8	4	0.2	
No final interpretation	69	74	0.08	1.24 (0.98-1.57)
Formal ultrasound				
Total patients	136	116	0.7	

n=number of patients

****: median (range)***

RR (95% CI): Relative Risk with 95% Confidence Intervals

There was no difference in the spread of the number of ultrasound examinations performed, but there was an increase in unnecessary scans in the study group even though the numbers were very small. As expected, there was no difference on the findings at formal ultrasound ($p=0.7$) since these were done by the same trained sonologists in both time periods.

However, there were significant differences in what was found during informal ultrasound examinations done by the gynaecology registrar on call. There was a non-significant trend to better reporting of the uterine content and there were significantly less reports of definite signs of an intrauterine gestation (GS or retained products of conception (RPOC) together: 60 vs 24, $p<0.001$, RR 0.46, 95% CI 0.31-0.70). There was no significant improvement in the reporting of signs of viability once a GS was seen. There was a significant change in the spectrum of uterine findings ($p=0.001$), the spectrum of adnexal findings ($p=0.006$) and the spectrum of free fluid noted ($p=0.05$). There was an improvement concerning documentation of other ultrasound features assisting in the accurate diagnosis of EP including the adnexal appearance and presence of free fluid, but no change in the number of reports lacking a final interpretation.

The results of all the requested beta-hCG levels are summarised in Table 5.

Table 5: Data on the performance and results of beta-HCG levels of the control and study patients

Beta-hCG	Controls n=178	Study patients n=157	p-value	RR (95% CI)
At presentation:				
N Patients with no hCG	24	34	0.05	1.60 (0.99-2.59)
N Patients with hCG	154	123	0.05	0.91 (0.82-1.00)
Necessary hCG	72	77	0.1	
Unnecessary hCG	77	40	<0.001	0.60 (0.43-0.81)
hCG of uncertain value ^f	5	6	0.6	
All visits included:				
N patients with hCG	166	132	0.007	0.90 (0.83-0.98)
N tests/patient*	1 (0-7)	1 (0-8)	0.5	
Total number of tests	302	261		
Necessary hCG				
N Patients	103	94	0.1	
N tests/patient*	1 (0-7)	1 (0-8)	0.2	
Total number of tests	200	199		
Unnecessary hCG				
N Patients	86	63	0.5	
Tests/patient*	0 (1-3)	0 (1-3)	0.3	
Total number of tests	102	72		
Patients with no hCG				
N Patients	12	25	0.007	2.36 (1.23-4.54)

n=number

****: median number (range)***

♪ : documented information inadequate to evaluate appropriateness of hCG

RR (95% CI): Relative Risk with 95% Confidence Intervals

The most obvious difference between the two periods was a reduction in the total number of beta-hCG levels requested at presentation with a significant reduction in the number of unnecessary beta-hCG requests.

Although there was no difference in the number of women with 0 or 1 test versus those with repeat tests (n=108 vs 70 in controls and n=94 vs 63 in the study group, p=0.9), there was a significant difference in the spread of the number of beta-hCG tests per patient with less repeat tests in the study group (p=0.021, not in table).

Results on the accuracy of EP diagnosis and the appropriateness of EP management at first visit are presented in Table 6. Management was seen as inappropriate when not done in accordance to the algorithm. There were no major differences apart from significantly fewer MVAs being performed after the intervention.

Table 6: Data on the diagnosis and management of the control and study patients at first visit

Diagnosis and Management	Controls n=178	Study patients n=157	p-value	RR (95% CI)
1st visit				
Inappropriate diagnosis	40	47	0.1	
Inappropriate management (insufficient information)	28 (2)	21 (3)	0.5	
Management at first visit				
Laparotomy	50	53	0.2	
Laparoscopy	2	2	0.9	
MVA	34	11	0.001	0.37 (0.19-0.70)
MTX	7	5	0.7	
Follow-up	76	74	0.4	
Discharge	8	9	0.6	
None	1	3	0.3	

n=number of patients

MTX: Methotrexate; MVA: Manual Vacuum Aspiration

RR (95% CI): Relative Risk with 95% Confidence Intervals

Results on time to final diagnosis and management of patients after final diagnosis are presented in Table 7. In terms of time to final diagnosis, in the stable patients there was no difference between the two periods when zero days were compared with one or more days ($p=0.4$), zero to one day versus two or more days ($p=0.8$), zero to one versus two to three days ($p=0.9$) and zero to three versus more than three days ($p=0.9$).

Concerning management of patients after the final diagnosis, again there were no major differences between the two periods apart from significantly fewer MVAs being performed after the intervention and more patients called back for follow-up after final diagnosis (expectant management of EP/pregnancy of unknown location (PUL)).

Table 7: Data on time to final diagnosis and management of the control and study patients

Diagnosis and Management	Controls n=178	Study patients n=157	p-value	RR (95% CI)
Time to final diagnosis				
Days to final diagnosis*	2.3 ± 4.2	2.8 ± 6.1	0.4	
Management after final diagnosis				
Ectopic Pregnancies	68	69		
Total laparotomy (+ MVA)	54 (1)	58 (2)	0.2	
Unstable	21	21	0.8	
Working hours	9	9	0.3	
After hours	43	49		
Time of day unknown	2	0		
Inappropriate	4	4		
Total laparoscopy (+ laparotomy)	3 (1)	4 (1)	0.6	
Unstable	0	0		
Working hours	2	2	0,6	
After hours	1	1		
Time of day unknown	0	1		
MVA	47	21	0.003	0.51 (0.32-0.81)
Additional with laparotomy	48	23	0.006	0.54 (0.35-0.85)
Inappropriate	2	1	0.6	
Total MTX (+ surgery)	12 (1)	6 (1)	0.2	
Unstable	0	0		
Working hours	2	2	0,6	
After hours	1	1		
Time of day unknown	0	1		
Inappropriate	1	2	0.5	
Follow-up	8	16	0.04	2.27 (0.99-5.15)
Inappropriate	2	2	0.4	
Discharge	43	44	0.4	
Inappropriate	8	4	0.2	
No notes	3	2	0.8	
DNA before final diagnosis	8	6	0.8	

**Data in number of patients (n); *: mean ± standard deviation
 MTX: Methotrexate; MVA: Manual Vacuum Aspiration; DNA: Did Not Attend
 RR (95% CI): Relative Risk with 95% Confidence Intervals**

Seventy one patients were stable at the time of laparotomy and could potentially have had a laparoscopy instead: 33/54 in the control group and 37/58 in the study group. There were eight inappropriate laparotomies (three could have had MTX) of which five were negative laparotomies (four patients).

Below is a brief discussion of the control group patients with inappropriate laparotomies:

- 1. A stable patient presented after hours with four weeks amenorrhoea, minimal pain and a positive pregnancy test. Informal ultrasound was documented as an EP with minimal free fluid (no other details were given), and her beta-hCG was 1745 mIU/ml. She had a negative laparotomy and a follow-up formal ultrasound two weeks later diagnosed an early intrauterine pregnancy (case 3).*
- 2. A stable patient presented with lower abdominal pain and a formal ultrasound suspicious of an EP (no intrauterine GS, adjacent to right ovary a mass with a cystic centre of 18x20mm and minimal free fluid). Her beta-hCG was 219 mIU/ml and after a consultant review a laparotomy was performed. A right corpus luteum cyst and a Morgagnian cyst were found in the right adnexa for which a salpingectomy was done. The left adnexa was normal (left tubal ligation was performed on patient request) and no free fluid was found in the pelvis. Her beta-hCG increased from 643 to 1465 mIU/ml in 48 hours post surgery and she was discharged with the diagnosis of an early IUP (no repeat ultrasound done). At a follow-up visit one week later she was stable but had ongoing lower abdominal pain, a beta-hCG of 8819 mIU/ml and a formal ultrasound was unchanged from her initial ultrasound (despite the cyst being surgically removed). After consultant review a second negative laparotomy was performed and the right corpus luteum cyst was drained. MTX was given post-operatively and an MVA was performed two days later. After a suspicious abdominal ultrasound, a dissecting aortic aneurism was diagnosed on CT (13 days after initial presentation) and the patient was urgently referred to the vascular surgeons. Histology of the evacuated tissue showed products of conception and her beta-hCG decreased appropriately from 2707 to 32 mIU/ml over two weeks (case 4).*
- 3. A stable patient presented after hours with five weeks of amenorrhoea, pain, vaginal bleeding and a positive pregnancy test. An informal ultrasound showed a right-sided mass with a diagnosis documented as a possible EP or ovarian cyst. Her beta-hCG was 812 mIU/ml and a laparotomy and salpingostomy of a right tubal pregnancy was done after hours with minimal blood in the pelvis found during surgery (case 5).*

Below is a brief discussion of the study patients with inappropriate laparotomies:

- 1. A stable patient presented after hours with vaginal bleeding (passing solid pieces and clots) and lower abdominal pain. Informal ultrasound findings were documented as RPOC and a right cystic heterogenous mass with no free fluid. Her beta-hCG was 2416 mIU/ml and a consultant decision was to do a laparotomy and an MVA. At laparotomy a right salpingectomy was done for a large tubal mass and the MVA was documented as very few but obvious products of conception. Only the tubal mass was sent for histology which showed no EP. The patient was not followed up (case 6).*
- 2. A stable patient presented within working hours with nine weeks of amenorrhoea, pain, vaginal bleeding and a positive pregnancy test. An ultrasound done by the referring general practitioner was documented as an EP in the left adnexa with no fetal heart. No further ultrasound results were documented and no beta-hCG was done. Consultant decision was a laparotomy. This was done after hours during which a left salpingectomy was performed and 200ml of haemoperitoneum was*

- found. There was no documentation whether medical management was offered to the patient or whether the EP was ruptured or not during laparotomy (case 7).
3. A stable patient presented after hours with six weeks of amenorrhoea, mild lower abdominal pain for one week, vaginal bleeding and a positive pregnancy test. An informal ultrasound showed a 22x16x25mm right adnexal mass with the right ovary seen separately. Her beta-hCG was 222 mIU/ml and a consultant decision was to proceed to a laparotomy (there was no documentation on whether medical management was offered to the patient), during which a 100ml of blood clots were found in the pelvis and a right salpingectomy was done for the tubal pregnancy (case 8).
 4. A stable patient presented on a Saturday with seven weeks of amenorrhoea, pain, vaginal bleeding and a positive pregnancy test. An informal ultrasound showed an empty uterus, no adnexal masses and no free fluid. Her beta-hCG was 30276 mIU/ml and as she was stable with minimal symptoms, a consultant decision was for follow-up. Although her beta-hCG more than halved in 48 hours to 9085 mIU/ml and her clinical condition remained unchanged, a formal ultrasound at that stage was suspicious of an EP (thickened endometrial lining (EL) of 11mm, hyperechoic mass of 17x18x15mm adjacent to the right ovary, minimal free fluid) and a consultant decided on a laparotomy and an MVA (done within working hours). She had a subsequent negative laparotomy and histology of the evacuated tissue later confirmed products of conception (case 9).

There were only seven laparoscopies performed in the entire cohort; three in the control group and four in the study group. They were all appropriate, but two were converted to a laparotomy.

1. The first patient (case 10) was diagnosed with a viable IUP at 10 weeks, but was acutely ill with nausea and vomiting and an adnexal mass on ultrasound. Due to her worsening clinical condition, surgery was indicated. The registrar diagnosed ovarian torsion during a laparoscopy, but did not feel comfortable with performing a laparoscopic salpingectomy and converted to a laparotomy.
2. The second patient (case 11) had a laparoscopy for a suspected EP, which was converted to laparotomy due to the EP being adherent to the anterior abdominal wall and colon.

Four patients (two control and two study patients) should have had laparoscopies instead of only being followed up:

1. A stable patient (case 12) presented with four weeks amenorrhoea, pain and a positive pregnancy test; a formal ultrasound showed an empty uterus, a right solid adnexal mass of 79x79x64mm and no free fluid; she was followed-up with serial beta-hCGs that decreased from 29 to 14 mIU/ml in 48 hours; due to her worsening clinical condition (increased pain and declining Hb) a laparotomy and salpingectomy were done for an EP three days after presentation. Documented findings were that of a chronic EP with old blood clots in the pelvis.
2. A stable patient (case 13) with 15 weeks of amenorrhoea, pain and vaginal bleeding; informal ultrasound showed an empty uterus, an adnexal mass of 36x33mm and a beta-hCG of 11980 mIU/ml; she was admitted for a follow-up ultrasound in 48 hours; formal ultrasound confirmed an EP of 48x42x39mm; she had a laparotomy for a ruptured corneal EP two days after presentation.
3. A stable patient (case 14) with 14 weeks amenorrhoea and vaginal bleeding; an informal ultrasound showed an empty uterus, a right adnexal mass of 28x20mm

(possibly an ovary) and no free fluid; although her beta-hCG was 5516 mIU/ml, a registrar decision was to review her in 48 hours when a subsequent beta-hCG was 7285 mIU/ml (a formal ultrasound confirming a left adnexal mass of 18x14x17mm); after consultant review the patient received MTX and needed a second treatment with MTX before responding to medical treatment.

- 4. A stable patient (case 15) presented with a positive pregnancy test, pain and vaginal bleeding; an informal ultrasound showed an empty uterus, a left adnexal mass of 42x43x38mm and a beta-hCG of 2431 mIU/ml; a registrar decision was to follow the patient up; the subsequent beta-hCG declined by more than 50% to 772 mIU/ml and the patient was discharged with the diagnosis of a complete miscarriage. She did not have a formal ultrasound to confirm or exclude the adnexal mass and there was no documentation of further visits to TBH.*

There were three patients treated inappropriately with MTX when a laparoscopy was indicated. The control patient (case 1) and study patient (case 14) were described earlier. *A study patient (case 16) presented with nine weeks amenorrhoea, pain and vaginal bleeding. A formal ultrasound showed an EL of 6.2mm, no adnexal masses and a possible subserosal fibroid. Her beta-hCG was 4104 mIU/ml and the consultant decided on medical treatment. The patient failed to return for follow-up.*

Two patients underwent surgery after medical treatment with MTX. The first case was discussed above (case 1). *The second case (case 17) was a 34-year old patient in the study group. She had one previous normal delivery with no other risk factors and presented with amenorrhoea for eight weeks and mild lower abdominal pain. A formal ultrasound showed a complex mass adjacent to the left ovary of 27x25x18mm with an empty uterus and moderate amount of free fluid. Her beta-hCG was 3515 mIU/ml and after consultant review, the decision was made for medical treatment. Unfortunately the EP growth was not interrupted with a single dose of MTX and her beta-hCG increased to 6278 mIU/ml in 48 hours and 9406 mIU/ml in 120 hours post MTX. Although she was stable enough for a possible second MTX, she found follow-up visits difficult to comply with and after consultant review she had a laparoscopic salpingostomy of an unruptured EP during working hours.*

Three additional patients could have been offered MTX (cases 5, 7 and 8, which were discussed earlier).

Two control patients and one study patient had an inappropriate MVA where follow-up was indicated (none of them had an obvious clinical diagnosis of a miscarriage):

- 1. A stable control patient (case 18) with eight weeks amenorrhoea and vaginal bleeding had an informal ultrasound documented only as no free fluid was observed. A formal ultrasound was not done and her beta-hCG was 7722 mIU/ml. Despite a clinical diagnosis documented as either a miscarriage or an EP, the patient was taken for an MVA and discharged thereafter. There were no notes on what was found at the MVA and no tissue was sent for histology. No further notes or special investigations done suggested a subsequent visit by the patient.*
- 2. A stable control patient (case 19) with a positive pregnancy test presented with vaginal bleeding and lower abdominal pain. An informal ultrasound was documented to show no IUP or EP (although no detail of the ultrasound was given), and a formal ultrasound was not done as she presented after hours. Her beta-hCG was 4609 mIU/ml. The diagnosis was documented as an incomplete miscarriage*

and the patient was taken for an MVA. There were no notes on clinical findings at the MVA and no tissue was sent for histology. No further notes or special investigations done suggested a subsequent visit by the patient.

3. A stable patient (case 20) in the study group presented with eight weeks amenorrhoea and vaginal bleeding. An informal ultrasound showed an EL of 9.4mm, normal ovaries and a left simple ovarian cyst. A formal ultrasound confirmed these findings. Her beta-hCG was 526 mIU/ml and although an IUP or EP was not yet excluded, the patient had an MVA. There were no notes on clinical findings at the MVA and no tissue was sent for histology.

A review of the study group showed that only 41% of these patients were diagnosed and/or treated according to the proposed algorithm.

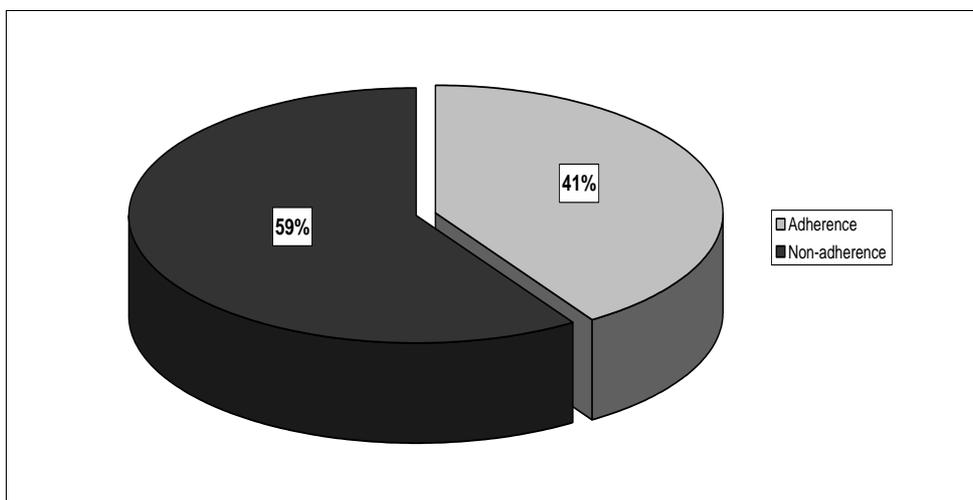


Figure 1: Adherence to the algorithm in the study patients

The results of the questionnaire (Addendum C) pertaining to the EP algorithm are summarised in Figure 2.

Responses were given to the following:

- Question 1: Do you know where the algorithm can be accessed or viewed?
- Question 2: Do you know what information the algorithm provides?
- Question 3: Did you use the algorithm?
- Question 4: If you used the algorithm, did you find it helpful?
- Question 5: Do you think the algorithm could be improved?

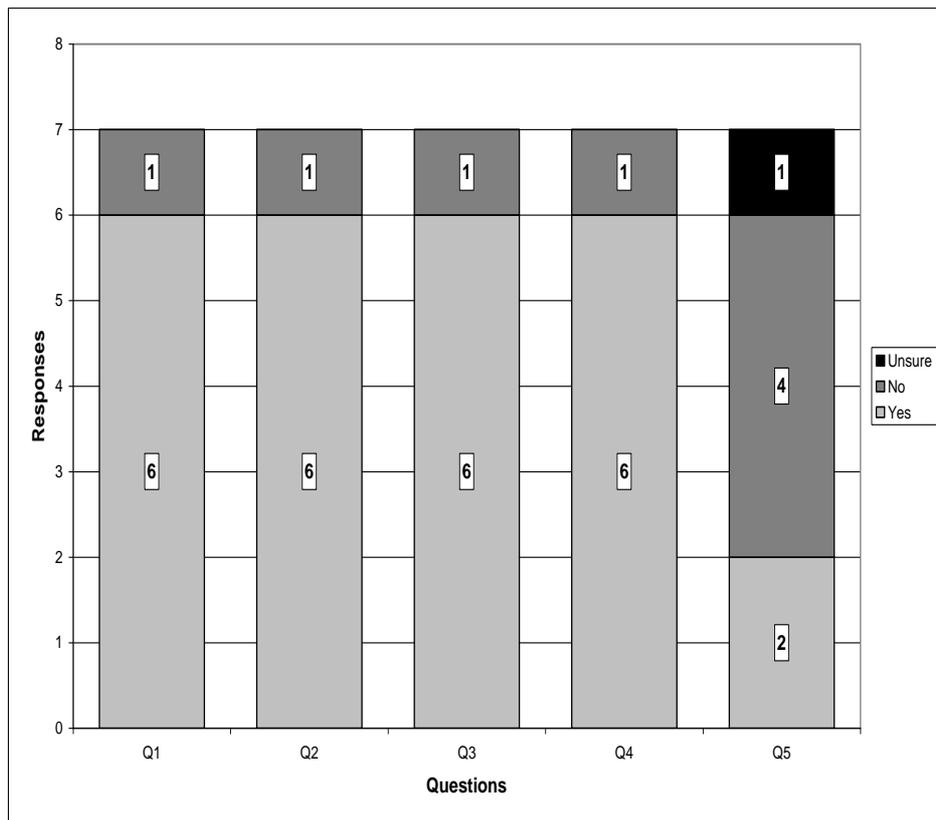


Figure 2: Answers to the questionnaire pertaining to the ectopic pregnancy algorithm

Individual comments and suggestions on improvement of the algorithm are discussed below.

The results of the questionnaire (Addendum C) pertaining to the ultrasound reporting form are summarised in Figure 3.

Responses were given to the following:

- Question 1: Did you know there is a gynaecological ultrasound reporting form?
- Question 2: Did you use the reporting form when performing an ultrasound?
- Question 3: If you used the reporting form, was it helpful?
- Question 4: Do you think the reporting form can be improved?

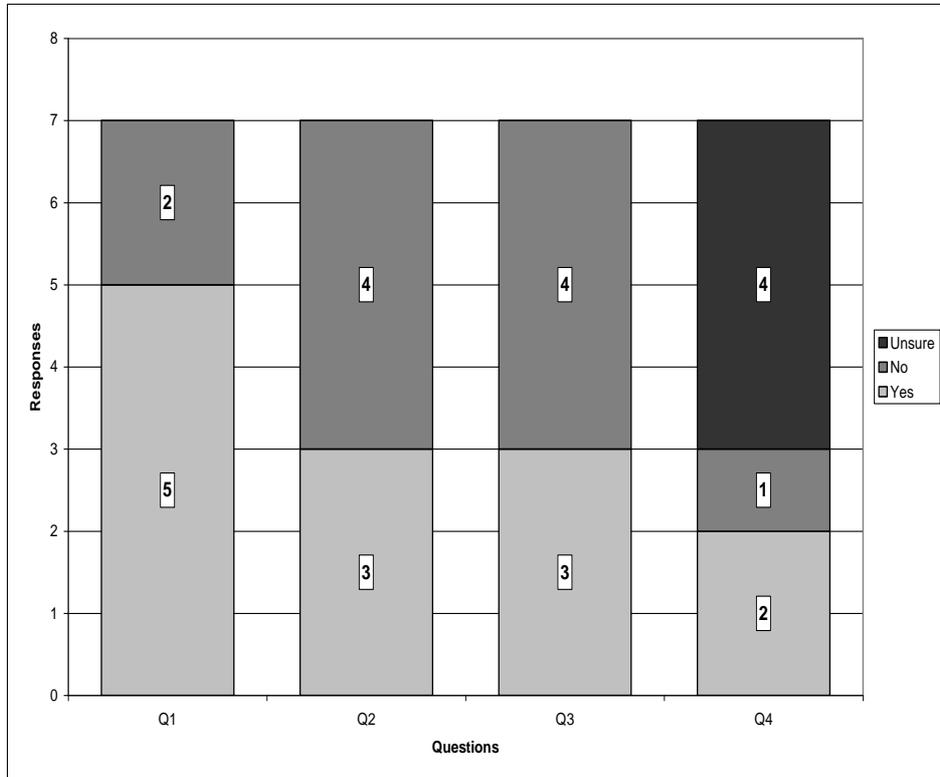


Figure 3: Answers to the questionnaire pertaining to the ultrasound reporting form

Individual comments and suggestions on the improvement of the reporting form are discussed below.

Discussion

This study showed that an educational intervention and diagnostic and management algorithm resulted in improved ultrasound findings by registrars and a reduction in inappropriate beta-hCGs at presentation and repeat beta-hCGs requested. Except for significantly fewer MVAs performed and more follow-up visits after the intervention, the improvement in special investigation usage did not translate into more accurate diagnosis or a significant difference in the management of suspected EP.

Delay in diagnosis

Mertz et al in 2001 compared the use of a strict diagnostic algorithm with an individualised approach in diagnosing EP. The patients diagnosed using the algorithm had a median diagnostic interval of two days, compared to eight days of those diagnosed with individual methods ($p < 0.001$). Tubal rupture rates (diagnosed at surgery) were significantly lower in the algorithm group (3.3%) compared to 23% in the comparative group ($p < 0.001$) with the obvious added benefit of a potential reduction in loss of reproductive function and mortality secondary to EP.⁽²²⁾

In a prospective study, Barnhart (1994) investigated a diagnostic algorithm combining quantitative B-hCG and TVUS. They found that the average time until diagnosis was a median of four days if the initial beta-hCG was below 1500 mIU/ml, and two days if the beta-hCG was above 1500 mIU/ml. This algorithm definitively diagnosed 78.8% of all patients on initial evaluation, reducing the number of patients in need of further intense follow-up.⁽¹⁹⁾

Gracia et al demonstrated that using TVUS as the first step in diagnosis, combined with quantitative B-hCG as indicated, was the most efficient and accurate method, diagnosing EP within an average of 1.46 days.⁽²¹⁾

This study showed no difference in the interval from presentation to diagnosis before and after the intervention with a median of 2.3 (± 4.2) and 2.8 (± 6.1) days to diagnosis respectively. Unstable EPs were diagnosed on the day of presentation. Unlike the studies of Mertz and Barnhart, which only included patients diagnosed with an EP, this study included all patients suspicious of an EP with a final diagnosis including any of the early pregnancy complications (symptomatic IUP/miscarriage/failing PUL/EP). Treatment included surgery, medical management and also follow-up (for patients diagnosed with a failing PUL or resolving EP managed expectantly) and discharge (e.g. an early IUP or complete miscarriage). Gracia's study only included stable patients, where this study also included unstable patients with an EP, managed with a laparotomy soon after presentation. None of the above studies commented on adherence to their protocols, where non-adherence to the algorithm in this study was high (59%). The lack of a reduction in the time to diagnosis after the intervention may therefore have been (partially) due to non-adherence to the protocol and not necessarily the protocol itself.

Special investigations

The study assessed whether the use of special investigations could appropriately be decreased by following an algorithm, therefore not only saving costs but hopefully also decreasing unnecessary follow-up visits and patient anxiety without compromising on an

accurate diagnosis and appropriate management.

1. Transvaginal ultrasound

The intervention at TBH improved the use of TVUS as the initial step to making an accurate and timely diagnosis. A few more unnecessary ultrasound examinations were performed (although very small numbers, 3 vs 12), but the quality of the informal ultrasounds done by registrars seemed to have improved in that pertinent parameters were assessed with more scrutiny.

Many studies show TVUS to be reliable in the diagnostic workup of women presenting with possible EP. In a UK study of 4255 women presented to an early pregnancy clinic, TVUS had a sensitivity of 89,9% and a specificity of 99,8% in diagnosing EP.(28) Other centres also concluded that non-surgical diagnosis of EP is superior due to the reliable prediction of EP with TVUS, and diagnostic laparoscopies should be limited to the small number of women with symptoms and normal ultrasonography.(29,30) TVUS also approaches 100% sensitivity in diagnosing 5.5 weeks IUP.(31,32) Although it is therefore widely accepted that TVUS has revolutionised the diagnostic approach of symptomatic early pregnancies, no studies have assessed the improvement in the quality of TVUS when using a diagnostic algorithm. The ultrasound reporting form accompanying the use of the algorithm as part of the intervention may have made a positive contribution in the current study since it was designed with the aim of guiding registrars in a detailed ultrasound assessment.

Garcia also reported an increase in the number of ultrasound examinations performed when using an algorithm combining an ultrasound followed by a beta-hCG if necessary, but this increase was associated with superior results (compared to the other five algorithms) in not missing any EP and not interrupting potentially viable IUP. Also, more timely diagnoses were achieved and fewer surgical procedures were necessary. (21)

In this study, the uterine content was reported more frequently and there was a significant change in the spectrum of uterine findings with significantly fewer reports of definite intrauterine gestations (*GS or RPOC*). This could indicate that registrars had more insight into the strict ultrasound criteria that need to be met for a fluid collection to qualify as an *intrauterine GS* and when another possibility should be considered for example a pseudosac. (Cacciatore concluded from a prospective study on 200 women in 1990 that a false positive diagnosis of IUP can be avoided if specific criteria are used for the definition of an intrauterine sac. (33))

Registrars probably also regarded *RPOC* with more caution and more often considered the possibility of a decidual reaction which could occur together with an EP.

Unfortunately there was no improvement in reporting viability in suitable cases (a fetal pole with a *GS* > 25mm and a fetal heart with the crown rump length (CRL) > 6mm) on documented early IUPs which could have been beneficial in dating an ongoing pregnancy and scheduling or avoiding repeat visits.

According to the proposed algorithm, an EP should have been considered and the adnexae assessed once the uterus was empty or had features of a possible pseudosac or decidual cast. This study demonstrated not only improved documentation of adnexal appearances, but also a change in the spectrum of adnexal findings and free fluid.

Despite these positive findings, there was no improvement in documenting the final interpretation of the ultrasound findings. It is difficult to determine whether this was due to a lack of insight or confidence into committing to a diagnosis, or whether it was only due to poor documentation. This was particularly disappointing since the ultrasound reporting form concludes with a concise and practical list of working diagnoses.

In a questionnaire (Addendum C) that was presented after the study to registrars working in the gynaecological unit during the study period, the following reasons were identified:

- Some registrars let the intern complete the ultrasound reporting form while they were performing the ultrasound examination and did not review the written report for correctness or completeness.
- Some registrars claimed not to have been aware of the reporting form. This is in spite of the compulsory attendance of the lecture by all gynaecology registrars, during which the algorithm and reporting form were demonstrated and in spite of both being distributed electronically to every member of staff of the department and the algorithm being displayed on the wall of the gynaecology admission area.
- Other registrars commented that the form was not always available in spite of the form being an official document printed by the hospital's printing services on simple request by the manager in charge of the clinical area.
- Some registrars admitted to being aware of the reporting form but forgetting to complete it.

Of the five registrars who were aware of the reporting form, three found it helpful, especially as they felt it served as a practical guideline for assessing early pregnancies.

2. Beta-hCG

This study showed a significant reduction in the number of beta-hCGs requested at presentation, the number of inappropriate beta-hCGs at presentation and the number of repeat beta-hCGs. There was still a considerable number (although not statistically significant) of unnecessary beta-hCGs in the study group and possible explanations for some of them could be the following facts stated by two of the registrars completing the questionnaire:

- Interns often requested beta-hCG levels before the registrar assessed the patient.
- Registrars requested the blood test pre-emptively on selected patients awaiting a formal ultrasound examination, since they found waiting for beta-hCG results could delay treatment. The HCG result may have been obsolete once the ultrasound findings were known.

Gracia et al also found that the diagnostic algorithm, using an initial TVUS followed by beta-hCG when necessary, decreased the number of blood tests compared to three other strategies involving beta-hCG, TVUS and progesterone in combination.⁽²¹⁾ To the author's knowledge there are no studies comparing the use of an algorithm to an individual approach in diagnosing and managing suspected EP with the number of beta-hCG tests as an outcome measurement.

Diagnosis

Despite the improved use of special investigations (TVUS and beta-hCG), this study showed no difference concerning inappropriate diagnosis before and after the intervention. Whether this was exclusively due to non-adherence to the algorithm or a lack of

documentation of pertinent findings at the time of clinical decision making (information therefore available to the clinician but not to the study) is difficult to determine. A diagnosis was often made on stable patients after hours, while these patients could potentially have waited for a formal ultrasound assessment the next morning, which could have contributed to an accurate diagnosis.

Barnhart's algorithm definitively diagnosed an EP in 78.8% of all patients on initial evaluation.⁽¹⁹⁾ As mentioned earlier, many studies concluded the high sensitivity and specificity rate of diagnostic algorithms. Sensible application of the non-invasive diagnostic methods is essential in making an accurate diagnosis, as guided by an evidence-based algorithm, but this requires adherence to the algorithm.

Similar to a study by Ankum in 1993⁽⁹⁾, analysis of cases with a false positive diagnosis of EP still suggests the need for expert sonographic skills. An example is case 3 discussed in the results section. This was a stable patient who could have waited for a formal ultrasound assessment instead of having a negative laparotomy.

Treatment

Except for significantly less MVAs being performed and an increase in the follow-up of patients in the study group (not inappropriately), there were no major differences in the management of study patients compared to the controls.

1. MVA

Gracia et al (21) found that there were 1% less potentially interrupted pregnancies when an algorithm, using ultrasonography followed by beta-hCG as indicated, was compared to two other algorithms where no EP was missed (beta-hCG and ultrasound as indicated vs ultrasound and follow-up ultrasound as indicated).

It is possible that the reduction in MVAs after the intervention was due to registrars being more aware of the differential diagnosis of the different ultrasound features which, combined with a beta-hCG below the discriminatory level, may have raised the possibility of an early IUP rather than RPOC. This may also have contributed to an increase in follow-up visits.

2. Follow-up visits

Spontaneous miscarriages that are not obvious at presentation (combining history, clinical assessment and ultrasound) and then subjected to our algorithm, could also have contributed to an increase in follow-up visits in our study group. Previous authors have shown that no diagnosis at first visit has a 17% chance of being an EP and an 11% chance of an IUP⁽¹⁷⁾, while another study reported a 14% chance of a patient ultimately diagnosed with an EP with an initial indeterminate ultrasound.⁽¹⁸⁾ Ankum found 19 of the 85 study population to have an early IUP with an initial inconclusive ultrasound and beta-hCG below the discriminatory zone.⁽³⁸⁾ One therefore needs to consider whether additional follow-up visits outweigh a potentially missed EP/IUP. In the majority of cases there should really only be one additional visit with a 48-hour beta-hCG follow-up to exclude an EP/early IUP when following the proposed algorithm.

In contrast to our finding of increased follow-up visits, Barnhart et al reported a reduction in the need for follow-up reviews as their algorithm had a 100% sensitivity and a 99.9% specificity in diagnosing EP in an emergency department.⁽¹⁹⁾ Their study only included follow-up patients diagnosed with an EP, in contrast to our study that included all patients suspected of having an EP and no definite IUP or miscarriage at presentation.

3. Surgery or medical management

One of the primary outcomes in this study was to evaluate the number of surgical procedures and medical treatment. Stoval et al showed that a diagnostic and therapeutic algorithm minimised surgical intervention with earlier diagnosis of EP, virtual elimination of diagnostic laparoscopy, greater use of MTX and increased use of expectant treatment. Of the 127 EPs in their study, 53 (41.7%) were treated with outpatient MTX. Three of the patients (5.7%) failed medical treatment and required surgery.⁽²³⁾

This study showed no significant difference in the number of patients having a laparotomy or laparoscopy or receiving MTX between the controls and the study group.

It was evident that the majority of patients diagnosed with an EP at TBH during this eight-month study period did not receive medical management due to late presentation and not due to ineffective healthcare. The results show no difference before and after the intervention of patients who should have been offered MTX as medical management (control group: case 5 vs study group: cases 7 and 8), with the numbers being obviously small.

Of the entire cohort, only 13.1% (18/137) of EPs could be managed medically, with no significant difference between the control and study group. One patient out of each group needed additional surgery.

What was of note is the small number of laparoscopies performed as definitive treatment after the educational intervention of this study presented guidelines from the RCOG⁽²⁵⁾ and a Cochrane review⁽⁸⁾ stating that a laparoscopic approach to the surgical management of EP, in a haemodynamically stable patient, is preferable to an open approach (safe, effective, outcomes equivalent to a laparotomy with lower costs, a shorter hospital stay, quicker return to normal activities, and radical or conservative procedures are possible and there is no increased risk to the patient with training staff)⁽⁷⁾. In the patient who is haemodynamically unstable, management should be by the most expedient method, and in most cases this will be a laparotomy.

More than half of the patients needing surgery in the control as well as the study group were stable when diagnosed with an EP and therefore in theory suitable for a laparoscopy. Unfortunately the infrastructure of TBH is not adequate to provide for unlimited laparoscopic theatre time. A shared theatre for obstetrical and gynaecological emergencies, registrars not being experienced in laparoscopic work and laparoscopic instruments not being available after hours often favours a laparotomy, which further contributes to less experience in laparoscopic surgery.

None of the studies evaluating the use of diagnostic and management algorithms commented on surgical preference. In a study done from October 1989 to September 1990, Stoval et al reported that of the 69 patients needing surgery as primary treatment, 21.7% had a laparoscopy and 78.3% had a laparotomy.⁽²³⁾ Gracia in 2001 only reported

laparoscopic treatment when surgery was indicated for an EP.⁽²¹⁾

The expectation was to see a reduction in inappropriate laparotomies, but there were equal numbers in both groups (eight in total). Non-adherence (59% in total) to our algorithm contributed to these results.

Use of the algorithm

1. Registrars' experience

In the questionnaire (Addendum C), six of the seven registrars knew that the algorithm could be accessed in the gynaecological emergency unit. They knew that it provided information pertaining to the diagnosis and management of EP, they used it and found it helpful. Individual comments were that the visual nature of the algorithm was helpful in teaching medical officers and interns as well as, in explaining to patients a possible diagnosis and management plan. Another registrar commented that it was useful to have cut-off values for ultrasound measurements and beta-hCG values and it was useful to have a formal local protocol for the workup and treatment of patients with a possible or proven EP (as provided in the algorithm). One registrar found it particularly helpful as it was easily accessible and logical, assisting in an often not clear-cut diagnosis. One registrar felt the algorithm could be improved by simplifying it and printing it on one page, whilst another appreciated the detail and thought it might be easier to follow if displayed on a single poster instead of separate A4 pages. The registrars felt they should have continuous training and feedback concerning the use of the algorithm and their clinical management of patients with symptomatic early pregnancies.

2. Adherence

Koh et al⁽³⁷⁾ reported much practice deviations from a protocol introduced to diagnose EP. They had 70% of non-adherence. Koh et al's study differed from this study in that qualified gynaecologists were the attending doctors. Most felt that the protocol would waste unnecessary time before a definite diagnosis and that patients may default to go to another doctor.

Despite the positive feedback from *registrars*, review of the raw data showed 59% of non-adherence to the algorithm. However, it should be taken into account that consultants usually make the final decision in terms of treatment, and that interns often see patients and request investigations before registrar review.

Of note is that consultant decisions on the final treatment were often not according to the proposed algorithm (all four inappropriate laparotomies in the study group were a consultant decision). Telephonic consultation (especially after hours) between registrars and consultants could have had the adverse effect of clinically significant information not being mentioned, asked for or taken note of. The consultant also often did not have the algorithm readily available unless he/she was physically present in the admissions area. Many consultants therefore used an individual approach which did not always lead to optimal management decisions. In the patient with the aneurism for example (case 4), it is the author's opinion that the number of special investigations, inpatient days and days to final diagnosis could have been decreased considerably if the proposed algorithm had been followed. A laparotomy could have been avoided altogether and medical

management or an evacuation under local anaesthetics could have been offered as treatment. The case also illustrates the importance to consider a differential diagnosis in stead of stubbornly sticking to a diagnosis that has been proven wrong twice before while missing, as in this case, a potentially life-threatening condition.

A Cochrane review⁽³⁴⁾ on “Do clinical guidelines reduce the gap between evidence and practice?”, stated that self-reported practice is likely to over-estimate the impact of guidelines compared to measuring actual practice. They also included a range of factors that could influence the adherence to clinical guidelines: compatibility of recommendations with values of healthcare professionals; recommendations that require minimal change are more likely to be complied with; and passive implementation strategies are less effective than the use of reminders or educational visits.

A Cochrane review⁽³⁵⁾ on “Why don't GPs follow guidelines?”, stated that the majority of interventions using guidelines produced modest to moderate effects. One of the reasons for not following guidelines was related to the guideline format. Similarly, Gagliardi et al⁽³⁶⁾ commented in a research protocol that the guideline format may influence accessibility and ease of use, which may overcome attitudinal barriers of guideline adoption.

Biases and limitations of the study

There are no apparent biases (selection, information or confounding) in this study.

Fewer study patients had an ultrasound examination or pregnancy test prior to presentation. The control group was therefore potentially at an advantage.

A possible limitation of the study is that an accurate sample size calculation was impossible since the background incidences of the outcome variables are entirely unknown. In this study, the overall background incidence of inappropriate diagnosis was 40/178 patients (22.4%), of inappropriate management 30/178 patients (16.9%) and of unnecessary special investigations 89/178 (50%) with some overlap in these outcomes between patients. A reduction of the most frequent of these outcomes from 50% to 25% or 30% would have required n=130 or 208 patients, which would render this study large enough. A reduction in inappropriate management from 15% to 10% would have required 1454 patients. Such a large number of patients was beyond the scope of this study, as it was only a pilot study to explore the impact of the algorithm and to serve as guidance for a bigger study in the future after the implementation of the algorithm has improved.

Conclusion

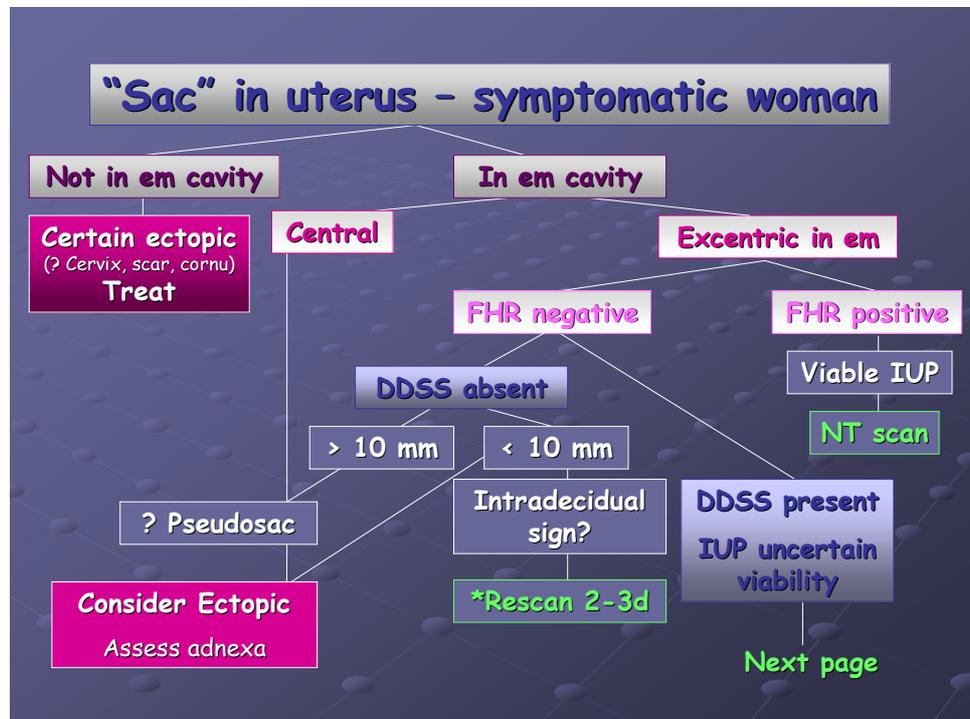
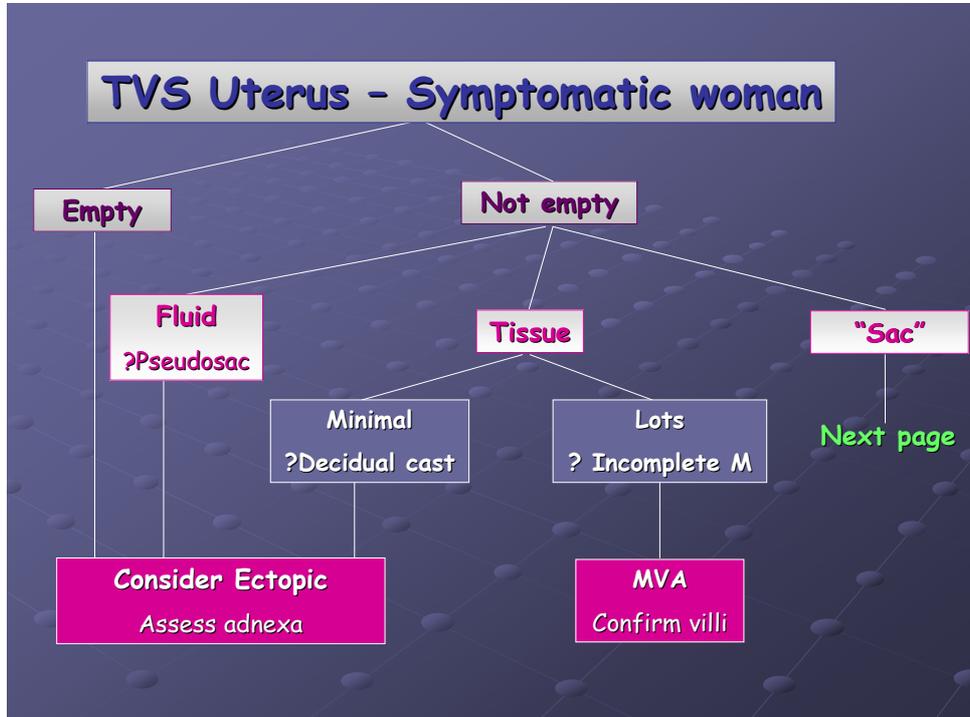
This study showed that an educational intervention and introduction of a diagnostic and management algorithm for EP in a busy Gynaecology Department at TBH resulted in the improvement of the quality of ultrasound examinations done by registrars, with increased awareness of signs pertaining to IUPs and possible EP. There was also a significant reduction in the number beta-hCGs requested (at presentation and at follow-up reviews) as well as a significant decrease in MVAs performed with possibly less interrupted early IUPs. The improvement in the use of special investigations unfortunately did not translate into fewer inappropriate diagnoses and management.

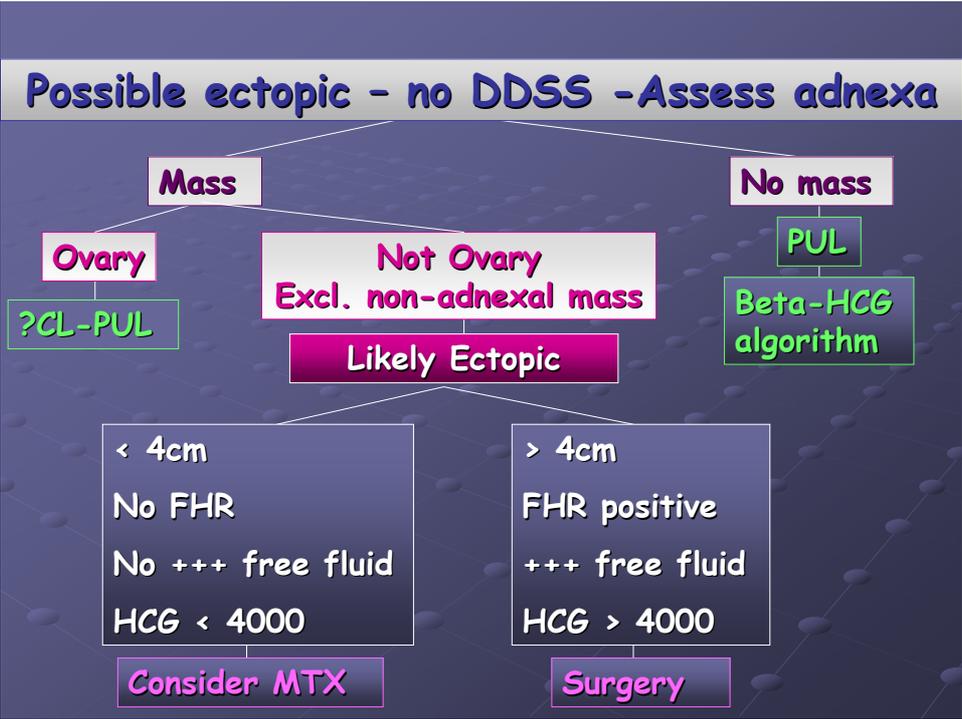
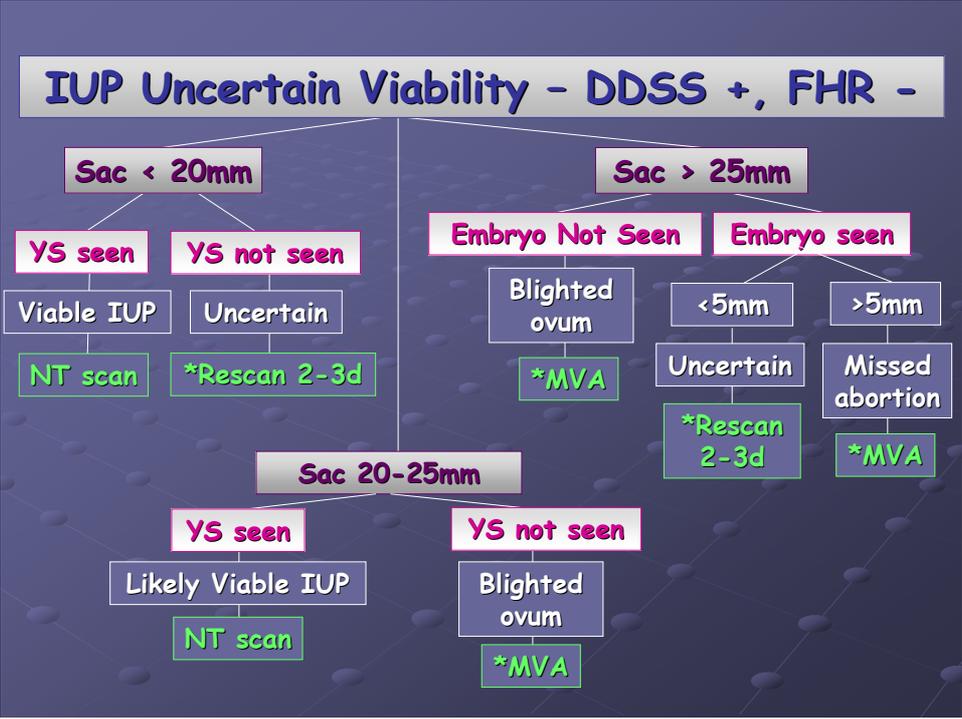
Some valuable information transpired from this study:

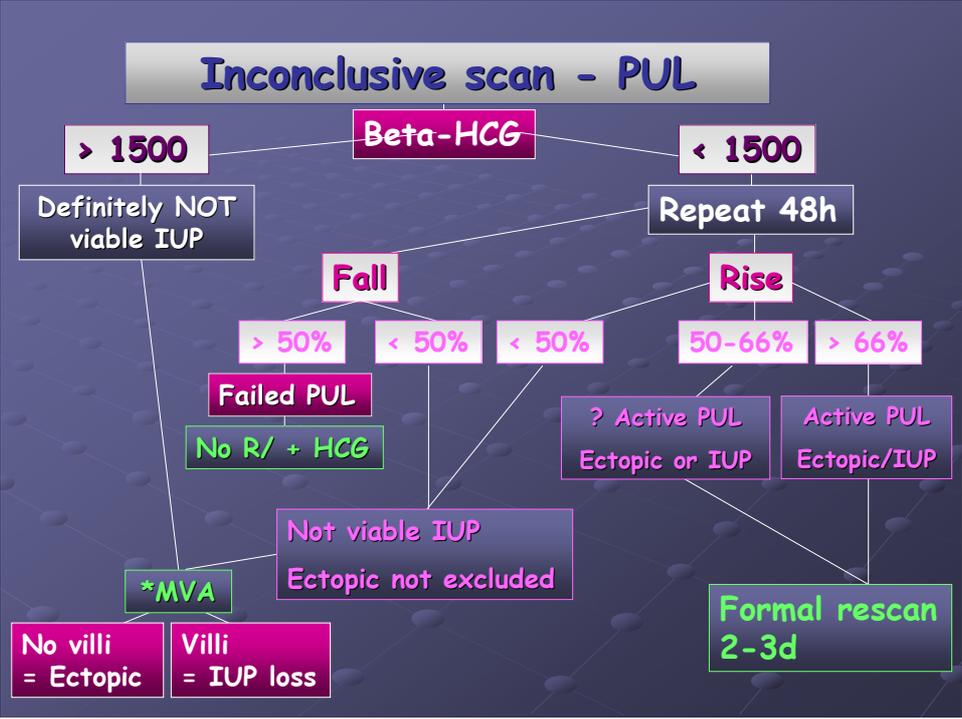
1. We made an assumption in the planning of this study that adherence to the proposed algorithm would be high. Adherence was essential to determine the algorithm's value but it was found that the algorithm was in the majority of cases not followed, either by the intern, the registrar or the consultant responsible for the final decision regarding management. From previous research, it is clear that algorithms have great potential to improve diagnosis, management and outcome of EP but any algorithm can only be effective when used consistently and correctly. From this study it is clear that just providing an algorithm is not sufficient to change clinical practice and that widespread implementation is required.
2. The study identified the need for ongoing training in the use of the algorithm, especially among new registrars and junior staff. Compulsory attendance of a computer-based slide series and completion of a test or case scenarios prior to commencing (or very early during) their first gynaecology rotation could achieve better knowledge, but adherence to the algorithm needs to be encouraged in the future and ensured on a continuous basis by the consultant on duty. Consultants need to be familiar with the algorithm and their involvement in all these cases should therefore be required. A formal audit of adherence with feedback to the different clinical teams may also be of benefit to improve adherence.
3. Constructive suggestions from the registrars for improvement were to display the algorithm onto a single poster and to incorporate the ultrasound reporting form into a gynaecology admissions booklet. This would avoid the form not being available or getting lost in an often less than adequate filing system.
4. Registrars also expressed the need for formal ultrasound training *earlier* in their rotations, followed by ongoing practical sessions to improve and keep up their skills. This would contribute to a more accurate diagnosis when relying upon their ultrasound findings after hours.
5. As the benefits of laparoscopic management of stable EP are numerous and as it is clear now that the majority of patients present early enough to qualify for laparoscopic treatment, investment in laparoscopic equipment and training of registrars and support staff is essential if women are to benefit from its advantages.

In conclusion, even though only a few positive results were achieved, positive and constructive feedback was received from registrars and the author is confident that ongoing education, continuous encouragement to adhere to the algorithm, and further improvements to the algorithm and its accessibility, would be beneficial towards the aim of providing better healthcare for patients with an at risk pregnancy.

Diagnostic and Management Algorithm for Suspected Ectopic Pregnancy







Addendum B

Patient sticker	Date:.....
	Doctor:.....

(please tick boxes or fill in numbers)

Early Pregnancy Ultrasound Report

Uterine content

Gestational sac	Seen		Not seen		
Location of sac	Corpus, central	Corpus,excentric	Cornu	Cervix	
Number of sacs				
Sac diametersmmmm mm	Mean:mm
Double decidual sign	Yes	No	Unsure		
Sac content	Empty	Yolk sac	Embryo	Unsure	
Sac contour	Regular		Irregular		
Embryo	Seen	CRL.....mm	FHR.....bpm	Not seen	
Content other than gestational sac	Empty		Fluid	Tissue	

Para-uterine findings

Free fluid in POD	No	Yes	Depth.....mm	Clear	Turbid
Left Ovary	Normal	Corpus Luteum	Mass:		
Next to left ovary	No mass	Mass	Describe and measure*		
Right Ovary	Normal	Corpus Luteum	Mass:		
Next to right ovary	No mass	Mass	Describe and measure*		

*:.....

Conclusion - Working diagnosis

Intact IU gestation*	Blighted ovum*	Missed abortion*	Molar pregnancy
Incomplete abortion	Complete abortion	Pregnancy of unknown location	
Possible ectopic	Certain ectopic~	Other:.....	

*: definitely no beta-HCG needed

~: beta-HCG only needed if medical treatment considere

Addendum C

Questions regarding the Algorithm for Suspected Ectopic Pregnancies:

1. Do you know where the algorithm can be accessed/viewed?

2. Do you know what information the algorithm provides?

3. Did/do you use the algorithm?

If yes, did/do you find it helpful and why?

If no, why not?

4. Do you think the algorithm could be improved and in what way?

Questions regarding the Gynaecological Ultrasound Reporting Form:

1. Did you know there is a gynaecological ultrasound reporting form?

2. Did you use it when performing informal ultrasounds?

If yes, did you find it helpful and why?

If no, why not?

3. Do you think the ultrasound reporting form could be improved and in what way?

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Abbreviations

CI	Confidence Interval/Vertrouensinterval
CRL	Crown Rump Length
EL	Endometrial Lining
EP	Ectopic Pregnancy
GL	Geerts,L
GS	Gestational Sac
IUP	Intrauterine Pregnancy
MTX	Methotrexate
MVA	Manual Vacuum Aspiration
O&G	Obstetrics & Gynaecology
PUL	Pregnancy of Unknown Location
RPOC	Retained Products of Conception
RR	Relative Risk/Relatiewe Risiko
SA	South Africa
TBH	Tygerberg Hospital
TVUS	Trans-vaginal Ultrasound
UK	United Kingdom
WP	Wipplinger, P