South African National Essential Medicine List
Primary Healthcare Medication Review Process
Component: Gynaecology

Date: 12 July 2016

Question: Can TOPs be accomplished safely and effectively without ultrasound?

Introduction/Background:
Currently the PHC EML does not include termination of pregnancy (TOP), even medical TOPs (≤ 63 days) in early pregnancy. The reasons for this include the following:

» Access to ultrasound has been mandatory up to this point:
    a. Pre-procedure:
        i. To accurately determine gestation age, for eligibility purposes
        ii. To exclude ectopic/ gestational trophoblastic disease
    b. 1-week post procedure:
        i. To confirm TOP complete
» Mifepristone is not currently a general PHC essential medicine (misoprostol is included for indication of PPH)
» Venues need to be accredited (see annexure 1. Amendment to TOP Act)

Is the lack of diagnostic US denying women access to termination of pregnancy care? This document aims to examine the available evidence regarding the feasibility, safety and efficacy of an approach that foregoes routine ultrasound, where not available.

Purpose/Question:
P - pregnant women seeking TOP [with gestation ≤ 63 days/ < 13 weeks]
I - clinical assessment alone [before and/or after procedure]
C - ultrasound [before and/or after procedure]
O - incomplete TOP, retained products, septic TOP, missed ectopic pregnancy, uterine rupture, uterus perforation, haemorrhage, missed gestational trophoblastic disease, increased mortality

Data sources: Pubmed
Search strategy:
((((((("ultrasonography"[Subheading] OR "ultrasonography"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasound"[All Fields] OR "ultrasonics"[MeSH Terms] OR "ultrasonics"[All Fields]) OR ("ultrasonography"[Subheading] OR "ultrasonography"[All Fields] OR "echography"[All Fields] OR "ultrasonography"[MeSH Terms] OR "echography"[All Fields])) OR ("ultrasonography"[Subheading] OR "ultrasonography"[All Fields] OR "ultrasonography"[MeSH Terms])) AND ("abortion, induced"[MeSH Terms] OR ("abortion"[All Fields] AND "induced"[All Fields]) OR "induced abortion"[All Fields] OR "abortion"[All Fields])) OR ("abortion, induced"[MeSH Terms] OR ("abortion"[All Fields] AND "induced"[All Fields]) OR "induced abortion"[All Fields] OR ("termination"[All Fields] AND "pregnancy"[All Fields]) OR "termination of pregnancy"[All Fields])) AND (((((("abortion, incomplete"[MeSH Terms] OR ("abortion"[All Fields] AND "incomplete"[All Fields]) OR "incomplete abortion"[All Fields] OR ("incomplete"[All Fields] AND "abortion"[All Fields])) OR ("abortion, septic"[MeSH Terms] OR ("abortion"[All Fields] AND "septic"[All Fields]) OR "septic abortion"[All Fields] OR ("septic"[All Fields] AND "abortion"[All Fields]))) OR (retained[All Fields] AND product?[All Fields])) OR ("pregnancy, ectopic"[MeSH Terms] OR ("pregnancy"[All Fields] AND "ectopic"[All Fields]) OR "ectopic pregnancy"[All Fields] OR ("ectopic"[All Fields] AND "pregnancy"[All Fields]))) OR ("uterine rupture"[MeSH Terms] OR ("uterine"[All Fields] AND "rupture"[All Fields]) OR "uterine rupture"[All Fields] OR ("uterus"[All Fields] AND "rupture"[All Fields]) OR "uterus rupture"[All Fields])) OR ("uterine perforation"[MeSH Terms] OR ("uterine"[All Fields] AND "perforation"[All Fields]) OR "uterine perforation"[All Fields] OR ("uterus"[All Fields] AND "perforation"[All Fields]) OR "uterus perforation"[All Fields])) OR uter?[All Fields] AND ("haemorrhage"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields]))) AND ("gestational age"[MeSH Terms] OR ("gestational"[All Fields] AND "age"[All Fields]) OR "gestational age"[All Fields])

Study	Study type	Setting	Population	n	Intervention/comparison	Results/Effect	Comment
Eligibility purposes: U/S for determining gestational age							
Blanchard et al, 2007[1]	Cross sectional study	South Africa: 3 provinces: - Gauteng - WC - Mpumalanga	Women attending the public sector services for TOP	673	(A) Comparing gestational estimates: 1. By women's estimates of pregnancy duration. 2. By date of last menstrual period (LMP). 3. By clinical exam 4. By ultrasound (B) Proportion of women in the 'caution zone' (≤ 8 weeks gestation by woman or provider estimate and >8 weeks by ultrasound)	Women's estimates of pregnancy duration were 19 days fewer than ultrasound estimates (95% CI = –27 to 63). Mean provider- and LMP-based estimates were two (95% CI = –30 to 35) and less than one day(s) (95% CI = –46 to 51) fewer than ultrasound estimates. Comparing provider and ultrasound estimates, 15% of women were in the 'caution zone'; this fell to 12% if estimates of 9 weeks or fewer were considered acceptable.	 Blanchard_compair son of womens prov
Bracken et al, 2011 [2]	Prospective trial	USA - 10 TOP clinics	- Pregnant women seeking TOP with mifepristone/misoprostil. - Limit of standard mifepristone/ misoprostil regimen used for early TOP is ≤ 63 days.	4484	(A)Comparing gestation estimates: 1. By dates (LMP) 2. Bimanual examination 3. Ultrasound (B) Proportion of women in the where gestation incorrectly underestimated around 63 day threshold.	1.6% (63/4008) women incorrectly accepted for treatment outside of limits of standard mifepristone/ misoprostil regimen (≤ 63 days).	 Bracken_et_al-2011-BJOG-_An_Internatic
Fielding et al, 2002[3]	Prospective trial	USA	Adult pregnant women seeking TOP in a trial sponsored by ARM (Abortion Rights Mobilization) of New York City.	1016	1. Gestation estimated by dates and bimanual examination compared to US. 2. Perception of whether US indicated (pre- and post procedure)	- Clinicians correctly assessed gestation ≤ 63 days in 87% of women. - Gestational age underestimated in 1% (14/1013) - In 7/24 (29%) women with persistent gestational sac, clinician did not indicate need for US when it was likely needed.	 Fielding_Fielding SL, Schaff EA, Nam N
Nichols et al, 2002[4] - *abstract only*	Observational study	USA	Pregnant women requesting TOP in 1st trimester	245	Gestation estimates by bimanual examination compared against ultrasound in faculty physicians and residents	Pelvic examination agreed with the ultrasound (± 2 weeks) in 92% of cases for faculty physicians and 75% for residents.	
Fakih et al, 1986[5] - *abstract only*	Observational study	USA	Pregnant women admitted for 1st trimester TOP	120	- Agreement between US and LMP - Agreement between US and bimanual	Disagreement (> 2weeks) between US and LMP: 14% Disagreement between US and bimanual examination: 13%.	

Study	Study type	Setting	Population	n	Intervention/comparison	Results/Effect	Comment
Ectopic pregnancy – indirect evidence searches							
Amoko et al, 1995[6] – *abstract only*	Cross-sectional study	South Africa	Pregnant women with ectopic pregnancies seen at Umtata General Hospital	148	Incidence, risk factors, clinical presentation and complications of ectopic pregnancy.	- Incidence of ectopic pregnancy was 11 per 1000 reported pregnancies, and the mortality rate was 2.0%. - Only four intact unruptured ectopics were found in spite of the availability of modern diagnostic techniques such as ultrasonography and sensitive pregnancy tests. - 86% of the cases had evidence of previous pelvic infection.	
Mol et al, 2002[7]	-	Amsterdam	Women at increased risk of ectopic pregnancy	-	Compare two screening programs: 1. At pregnancy diagnosis, a transvaginal ultrasound, serum hCG measurement and serum progesterone or a combination of these tools done. 2. 'Watchful waiting' program: investigations only done if symptomatic.	Screening for ectopic pregnancy reduces the number of patients with tubal rupture, but only at the expense of a large false-positive rate. Although sonography in symptom-free women at risk of ectopic pregnancy might be justified for psychological reasons, the medical and economic benefits of such a policy seem to be limited.	
Incomplete TOPs - indirect evidence searches							
Ulmann et al, 1992[8]- *abstract only*	Large scale trial	France	11-48 year old women	16,173	Trial using mifepristone (RU 486) followed by the administration of a prostaglandin (PG) analogue for the medical termination of early pregnancy.	- The success rate of 95.3%. - 89.7% of the women bled for no more than 12 days. The bleeding was so profuse in 0.8% of the cases that either vacuum aspiration or dilatation and curettage was needed. 11 women required 1-3 units of blood.	
Fiala et al, 2003[9]	-	Austria	Women with an unwanted pregnancy below 49 days of amenorrhoea,	217	Ultrasound examination and serum hCG test were performed before treatment and at follow-up	N ongoing pregnancies: 2 Sensitivity (95% CI): 100.0% (19.7%–100%) Specificity (95% CI): 98.1% (95.0%–99.4%) PPV (95% CI): 33.3% (6.0%–75.9%) NPV (95% CI): 100.0% (97.8%–100%) Screen-positive: 2.8%.	
Grossman et al, 2007[10]	-	Mexico	Pregnant women, women with spontaneous abortions and women post-abortion	97	Compared the diagnostic accuracy of semi-quantitative urine pregnancy test to serum β-hCG testing.	Sensitivity of the urine test to identify individuals with a serum β-hCG level >1000 IU/L was 88.6% (95% CI 74.6– 95.7%), and its specificity was 71.7% (95% CI 57.4–82.8%).	
Selective US pre- and/or post- procedure: experiences in other countries Indirect evidence searches							
Silvestre et al, 1990[11]	-	France	Women seeking voluntary termination	2115	Effect of a single mifepristone followed by prostaglandin	The overall efficacy rate was 96.0 percent (95 percent confidence interval, 95.0 to 96.8). The	***Indirect observation*** - Selective pre-procedure

			of pregnancy after 49 days of amenorrhea or less. (selective ultrasound used)		analogues in terms of efficacy (failure) and safety.	failures included persisting pregnancies (1.0 percent), incomplete expulsions (2.1 percent), and the need for haemostatic procedure (0.9 percent). Most women had transient abdominal pain after receiving prostaglandin, but there were few other side effects.	US in 1st trimester, only performed in the case of discrepancy between LMP and uterine size, bleeding or symptoms indicative of an ectopic pregnancy, has been reported as being both safe and effective when patients are cared for by experienced clinicians[12].
Coyaji et al, 2001[13]	-	India: Urban: (Pune + Mumbai) Rural: Vadu	Women seeking abortions < 63 days gestation (based on LMP) or < 56 days or less in Vadu. (< 10% access to US)	900	Safety, effectiveness and acceptability of medical abortions in urban and rural hospitals in Inda.	- Ongoing pregnancy at study end 1%, 3.5%, 2,7% at Pune, Mumbai and Vadu respectively. - Incomplete abortion at study end 3.5%, 3.5%, 1% at Pune, Mumbai and Vadu respectively. - Medically indicated surgical intervention during study 0%, 1%, 0.3% at Pune, Mumbai and Vadu respectively.	
Abbasi et al, 2008[14]	Retrospective study	Iran	Women admitted for suspected RPOC after spontaneous first trimester miscarriage who were evacuated surgically, and for whom histopathological reports were available.	91	Clinical and sonographic findings were compared with the histo-pathological reports and the sensitivity and specificity of vaginal bleeding, abdominal pain and sonographic appearance of the endometrium for detecting the products of conception were assessed.	Vaginal bleeding as a predictor of RPOC had a sensitivity of 93%, specificity of 50%, and positive and negative predictive values of 74% and 82%, respectively.	

Systematic reviews

- Kulier R, Kapp N. Commprehensive analysis of the use of pre-procedure ultrasound for first- and second- trimester abortion. Contraception. 2011[15]
- Grossman D, Grindlay K. Alternatives to ultrasound for follow-up after medication abortion: a systematic review. [16]

International Guidelines:

The Royal College of Obstetricians and Gynaecologists: Best practice in comprehensive abortion care - 2015	https://www.rcog.org.uk/globalassets/documents/guidelines/best-practice-papers/best-practice-paper-2.pdf
The American College of Obstetricians and Gynaecologists: Best practice in comprehensive abortion care - 2014	http://www.acog.org/~/media/Practice%20Bulletins/Committee%20on%20Practice%20Bulletins%20--%20Gynecology/Public/pb143.pdf?dmc=1&ts=20140703T1932230602
WHO: 1. Safe abortion: technical and policy guidance for health systems 2. Safe abortion: technical and policy guidance for health systems Evidence summaries and GRADE tables 3. Clinical practice handbook for safe abortion. 2014 4. Health worker roles in providing safe abortion care and post-abortion contraception. 2015 "Recommendation 12: ultrasound use prior to induced abortion. Use of routine pre-abortion ultrasound scanning is not necessary. (Strength of recommendation: strong) Remark: The quality of the evidence based on a randomized controlled trial and observational studies is very low."	http://www.who.int/reproductivehealth/publications/unsafe_abortion/en/
NICE guidelines – refer to RCOG above	

Observations from evidence:

- Importantly, these studies did not address assessment beyond the 1st trimester where accurate gestational age assessment may be more important when choosing the appropriate abortion procedures.
- Selective pre-procedure US in 1st trimester, only performed in the case of discrepancy between LMP and uterine size, bleeding or symptoms indicative of an ectopic pregnancy, has been reported as being both safe and effective when patients are cared for by experienced clinicians. Signs or symptoms of ectopic pregnancy or risk factors (previous ectopic pregnancy, previous PID, IUD in place) [(12)].
- In staff less experienced in clinical examination, ultrasound seems to be helpful in assessing accurate gestational age.

Recommendations:

Suggest that 1st trimester TOP recommendations are added to the revised PHC EML with the following stipulations attached:

- Medical and surgical TOPs limited to **1st trimester** TOPs only (as with management of incomplete miscarriages), at **accredited facilities** only.
- Suggest that US is recommended, but not essential, if unavailable, except in the following cases:
    - Discrepancy between LMP and uterine size i.e: if uterus palpable abdominally (gestation likely to be ≥13 weeks or molar pregnancy)
    - Signs/symptoms or risk factors for an ectopic pregnancy: vaginal bleeding and/or pelvic pain, cervical motion tenderness, adnexal mass, previous ectopic pregnancy, previous PID or IUD in place.
    - Signs/symptoms of incomplete TOP (bleeding persists ≥ 7 days, any signs of sepsis) or failed TOP/continued pregnancy (conceptus not expelled after medical TOP, only minimal bleeding after TOP treatment, ongoing symptoms of pregnancy).
- Additional recommendations around STIs, Pap smears, post TOP contraception should be included.
- Rh negative patients should receive anti-D.

References:

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5. Fakih MH. The value of real time ultrasonography in first trimester termination. Contraception. 1986;33(6):533-8.
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12. Maureen Paul ES, Mark Nichols. The roles of clinical assessment, human chorionic gonadotropin assays, and ultrasonography in medical abortion practice. Am J Obstet Gynecol 2000;183(S34-S43).
13. K Coyaji BE, U Krishna, S Otiv, S Ambardekar, A Bopardikar, V Raote, C Ellertson, B Winikoff. Mifepristone abortion outside the urban research hospital setting in India. The Lancet. 2001;357.
14. S. ABBASI AJ, L. ESLAMIAN , V. MARSOUSI. Role of clinical and ultrasound findings in the diagnosis of retained products of conception. Ultrasound Obstet Gynecol. 2008;32(704-707).
15. Regina Kulier NK. Commprehensive analysis of the use of pre-procedure ultrasound for first- and second- trimester abortion. Contraception. 2011;83(30-33).
16. Grossman D GK. Alternatives to ultrasound for follow-up after medication abortion: a systematic review. Contraception. 2011;83(6):504-10

Annexure 1: Accredited facility as defined in the Termination of Pregnancy Act.

3. Place where termination of pregnancy may take place

(1) Termination of a pregnancy may take place only at a facility which—

- (a) gives access to medical and nursing **staff**;
- (b) gives access to an **operating theatre**;
- (c) has appropriate **surgical equipment**;
- (d) supplies **drugs** for intravenous and intramuscular injection;
- (e) has **emergency resuscitation equipment** and access to an emergency **referral centre** or facility;
- (f) gives access to appropriate **transport** should the need arise for emergency transfer;
- (g) has facilities and equipment for **clinical observation** and access to **in-patient facilities**;
- (h) has appropriate **infection control** measures;
- (i) gives access to safe **waste disposal** infrastructure;
- (j) has **telephonic** means of communication; and
- (k) has been **approved** by the Member of the Executive Council by notice in the Gazette.

(2) The Member of the Executive Council may withdraw any approval granted in terms of subsection (1)(k).

(3)

- (a) Any health facility that has a 24-hour maternity service, and which complies with the requirements referred to in subsection (1)(a) to (j), may terminate pregnancies of up to and including 12 weeks without having to obtain the approval of the Member of the Executive Council.
- (b) he person in charge of a health facility contemplated in paragraph (a) must notify the relevant Member of the Executive Council that the health facility has a 24-hour maternity service which complies with the requirements referred to in subsection (1)(a) to (j).

(4) The Member of the Executive Council shall once a year submit statistics of any approved facilities for that year to the Minister.

(5) Notwithstanding anything to the contrary in this Act, the Minister may perform any of the functions that the Member of the Executive Council may or must perform, if it is necessary to perform such function in order to achieve any of the objects of this Act.''.