Diagnostic accuracy and outcomes of ultrasound in the first trimester of pregnancy for detection of complications relevant for Austrian population, exclusive of screening for Down syndrome: A Systematic Review

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Creating the PICO questions

Ultrasound examinations performed in the first trimester of pregnancy – followed up by immediate action - should assist in the detection and / or avoidance of disorders which can harm mother or child during pregnancy, delivery or in the postnatal period. However, an unmanageable number of different possible disorders can appear and not all of them can be dealt with in the framework of one single review.

To create relevant PICO (Person – Intervention – Control – Outcome) questions two methods were used and assembled:

- Evaluation of existing data from the Austrian Social Insurance about inpatient treatment categorised by ICD-10 diagnosis and extraction of the most frequently treatment reasons around pregnancy, delivery and perinatal period.
- Sensitivity and specificity of Ultrasound Examination in pregnancy documented in literature. The research question asks for indications in the field of preventing pregnancy complications for which existing calculations and values of sensitivity and specificity are available.

Evaluation of existing data

Following diagnoses were included as relevant: O 0-99, P 0-96, Q 0-99.

The number of treated patients according to the listed diagnosis was ranked for frequency, separated by cases of hospital discharge and cases of death.

ICD 10 O 80-84 (*delivery)* was excluded. The most frequent cases for treatment in Austria 2004 were evaluated.

Out of the twelve most frequent diagnoses of discharge the frequency was evaluated in the differentiated level of ICD 10. For creation of the PICO question which enlightens an exigence of preventive ultrasound examination in different episodes of pregnancy the complications of delivery and injuries during delivery are necessary to exclude.

Therefore the diagnoses (ICD 10) O 70 (Perineal laceration during delivery), O 47 (False labour), O 42 (Premature rupture of membranes) and O 71 (Other obstetric trauma) were excluded. The remaining six diagnoses with frequencies > 5,000 in

2004 in Austria are listed in Tab. 1. Tab 2 are shows the cases of death occurred due to theses diagnoses. The group of preterm birth (P07) is the most frequent with 193 cases of death.

Tab. 1

ICD 10	Number 2004	Description
AD_Q99	**12.366**	Other chromosome abnormalities, not elsewhere classified
AD_O02	**7.058**	Other abnormal products of conception
AD_Q61	**6.901**	Cystic kidney disease
AD_P07	**5.992**	Disorders related to short gestation and low birth weight, not elsewhere classified
AD_O69	**5.630**	Labour and delivery complicated by umbilical cord complications
AD_O36	**5.627**	Maternal care for other known or suspected fetal problems

Tab. 2

ICD 10	Cases of Death 2004	Description
AD_Q99	**0**	Other chromosome abnormalities, not elsewhere classified
AD_O02	**1**	Other abnormal products of conception
AD_Q61	**65**	Cystic kidney disease
AD_P07	**193**	Disorders related to short gestation and low birth weight, not elsewhere classified
AD_O69	**0**	Labour and delivery complicated by umbilical cord complications
AD_O36	**0**	Maternal care for other known or suspected fetal problems

For prevention idea several categories of diagnoses must be distinguished:

- Disorders which are frequent but not lethal (Q 99, O 36)
- Disorders which endanger the mother's life (O 02)
- Disorders which endanger the infant's life (Q 61, P 07)
- Complications during delivery which were not associated with fatality in 2004 in Austria (O 69)

Resulting PICO questions out of the Austrian epidemiology:

- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters for detection and prevention of other chromosome abnormalities, not classified elsewhere, (Q 99)
- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters for detection and prevention of other abnormal products of conception(O 02)
- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters for detection and prevention of infant cystic kidney disease (Q 61)
- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters

for detection and prevention of increased risk of disorders related to short gestation and low birth weight, not elsewhere classified (P 07)

- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters for detection and prevention of possible labour and delivery complicated by umbilical cord complications (O 69)
- Ultrasound in first trimester of pregnancy versus ultrasound in later trimesters for detection and prevention of other known or suspected fetal problems (O 36)

Sensitivity and Specificity of Ultrasound Examination in pregnancy

For creating the PICO questions all preventive indications with best values for sensitivity and specificity should be included. That means all these evident factors able to predict highest probability for detection by ultrasound in first trimester of pregnancy.

The search was performed using Reference Manager.

Searchterm 1:

Sensitivity AND Specificity AND Ultrasound AND Pregnancy (11.5.2006)

Results: 6 Items

Kahyaoglu (2006)[1]

Shock index (SI) and predictive score grading system including it for predicting medical treatment failure of tubal pregnancies have been studied. Shock index was calculated as the ratio of heart rate to systolic arterial pressure. A predictive score was used based on four parameters including initial level of beta-human chorionic gonadotropin (betahCG), aspect of the image on ultrasound, size of the ectopic mass and shock index value at admission. The cut-off shock index value for tubal rupture was 0.77 with 89% sensitivity and 61% specifity. Study size was n=88. Results: it was demonstrated that tubal pregnancy patients who were managed with nonsurgical measures at admission and who had SI values lower than 0.77 and predictive score grades greater and equal to 6.5 did not experience tubal rupture and did not need surgical intervention during nonsurgical management.

Biedermann (2004)

Was excluded because of failed aim (content: ultrasound for breast examination)

Bloeckle (1994)[2]

To evaluate the use of serial measurement of cervical length and width of internal os by means of vaginal ultrasound 144 pregnant women were examined prospectively. Sensitivity of vaginal ultrasound examination between 20 and 27 weeks indicating the whole pathologic collective was only 30%, whereas up to 55.5% of pregnancies complicated by cervical incompetence were detected. Specificity (up to 95%) and

negative predictive value (90%) were high. The results show that cervical examination by vaginal ultrasound allows early detection of developing cervical incompetence. The high specificity and the high negative predictive value may be useful to exclude cervical incompetence in clinically unclear cases thus helping to avoid unnecessary therapeutical interventions.

Hoffmann (1990)[3]

Using pulsed Doppler, blood flow in the cerebral arteries was measured to assess the fetal central circulation. The Pulsatility-Index (PI) was calculated as a qualitative parameter of flow velocity waveforms. In 418 normal singleton pregnancies we performed 558 measurements between the 27th and 40th week of gestation to get normal range values of the PI. The curve shows a small decrease in the observed interval. In cases of an intrauterine hypoxia the resistance of the central vessels decreased to render the distribution of the fetal blood volume. This results in a centralisation of the fetal circulation. 131 high risk pregnancies were investigated and in 21 cases such a centralisation was registered. The fetal outcome of these fetuses was significantly worse compared with fetuses having a normal central flow resistance. We found for example a higher rate of caesarean sections because of fetal distress when the Pulsatility-Index was below the 5th percentile. The sensitivity of the method in prediction caesarean section for fetal distress was 59.3%, the specifity 95.3%.

Hitschold (1988)[4]

130 women with postterm pregnancies (281-297 days of gestation) were examined with pulsed Doppler ultrasound of an umbilical artery. The result was not included in clinical decisions. In the group with abnormal flow a high rate of cesarean sections because of fetal distress (53%) was necessary, whereas only 3% were performed in the group with normal flow. In cases with reduced enddiastolic blood flow velocity the fetal outcome was significantly worse compared with cases with normal flow. The sensitivity of pulsed Doppler ultrasound in predicting cesarean section for fetal distress was 71%, the specificity 91% (3 days before delivery). The oxytocin challenge test indicated this with a sensitivity of 58% and a specifity of 82%, whereas the nonstress test is not useful in predicting fetal risk in postterm pregnancy.

Sudik (1982)[5]

From January 1980 to July 1981 817 pregnant women were checked by means of an ultrasonic screening programme. Ultrasonic measurement of the BPD and of the thoracic diameter were performed in the first trimester between 21 and 30 and 31 and 40 weeks of gestation. The Prenzlau and Issel diagram was used for evaluation. 72 out of the 817 women delivered a child with a birthweight below the 10th centile (GDR-Standards). From these children 65 (90,3%) were antenatally detected by ultrasonography. Hence, the sensitivity of the screening programme was 90,3%. The other parameters of the screening were: specificity 97,7%, positive predictive value

79,3%, negative predictive value 95,2%, effectivity 97,1%. The prediction of intrauterine growth retardation in the screening was significantly better compared to a group of 90 growth retarded children whose mothers were only examined by sonography sporadically. The average detection rate in both ultrasonic groups was 83,3%, but in contrast the percentage of clinically detected small-for-dates infants was only 15,4%.

Searchterm 2:

Sensitivity OR Specificity AND Ultrasound AND Pregnancy (12.5.2006)

3,172 Items à Limits *only items with abstracts, humans, 2 years à* 368 Items, the first 200 included

Studies were selected by title, studies with relation to Combined Test were excluded[6]. Studies were selected by abstract, studies with non relevant content were excluded[7]. (Ultrasound in emergency room – not with pregnancy).

The resulting studies include 25 with description of sensitivity and/or specificity of ultrasound examination (and in combination with other diagnostic methods as an index).

Indications for ultrasound examination were in three studies fetal growth reduction, in one study fetal weight > 4kg, in three studies fetal malformations, in three studies fetal heart diseases, in five studies other abnormities, in four studies diagnosis of preterm birth, in two studies preeclampsia, and in one study each detection of ectopic pregnancy and test of twin chorionicity (monochorional, bichorional) and umbilical. blood flow[8].

Studies without description of sensitivity or specificity in the abstract included following themes: malformations (16), cervix length and risk of preterm birth (11), fetal anaemia (6), preeclampsia (6), fetal outcome (6), fetal growth (5), ectopic pregnancy (5), fetal heart disease (5), detection of gestational age (5), placenta insufficiency and placenta previa (4), macrosomia (3), preterm prognosis (3), IVF aftercare (2), time point for labour induction (2), nuchal fold for gestational diabetes (2), prognosis of complications during pregnancy (2), cysts or tumors in pregnancy (2), twin complications (2), fetal activity (2), miscarriage (2), fetal face analysis (2), risk detection for sectio (1), fetal thoracic excursions (1), fetal reflex analysis (1), fetal gastric content (1).

For creation of the PICO question for ultrasound in first trimester of pregnancy following indications seem to be not relevant:

- fetal gastric content
- fetal reflexes
- fetal thoracic excursions
- fetal face analysis

- fetal activity
- time point for labour induction
- IVF aftercare

The terms of *fetal outcome* and *prognosis of complications* are very common and broad. They might be included in more detailed diagnostic measurements.

For the PICO question remain following indications:

On the mother's side:

- Ectopic pregnancy
- Preeclampsia
- Placentainsufficiency
- Miscarriage
- Cysts and Tumors
- Diabetes

On the fetal side:

- Gestational age
- Malformations
- Risk of preterm birth
- Growth
- Anaemia
- Twin complications
- Macrosomia

Miscarriage, malformations and risk of preterm birth were evaluated as relevant indicators out of the existing data in Austria.

Thus prior selected indicators are ectopic pregnancy, preeclampsia, gestational diabetes, gestational age and fetal growth.

Placenta insufficiency and fetal anaemia seem to be not detectable in first trimester of pregnancy. Cysts and tumors are less probable and therefore not in front ranks of indications to include.

Resulting PICO questions out of the described thoughts and research:

- Ultrasound in first trimester of pregnancy versus ultrasound in later pregnancy for detection or prevention of ectopic pregnancy complications.

- Ultrasound in first trimester of pregnancy versus ultrasound in later pregnancy for detection or prevention of preeclampsia
- Ultrasound in first trimester of pregnancy versus ultrasound in later pregnancy for detection or prevention of gestational diabetes
- Ultrasound in first trimester of pregnancy versus ultrasound in later pregnancy for detection or prevention of gestational age.
- Ultrasound in first trimester of pregnancy versus ultrasound in later pregnancy for detection or prevention of abnormal fetal growth.

The considerations for the PICO questions were basic for the EBHVB peer group's discussion for final selection of the PICO's for the envisaged review.

As a result of the discussion within the department and with clinical experts it was decided to exclude the diagnosis of cystic kidney disease (Q61) due to little relevance. Also the detection of gestational diabetes to be detected by means of ultrasound in the first trimester was discussed controversially. Gold standard is the oral glucose-tolerance-test in the second trimester. Due to the method of interpretation of nuchal translucency as a risk of gestational diabetes which was described in some studies (which built the basis for developing the PICO questions), and nuchal translucency as a prior method of measurement in the first trimester ultrasound the project team decided to include this PICO question and check on the results.

Experts suggested the detection of twin pregnancies as an important argument for the integration of an additional ultrasound examination in the first pregnancy trimester into the screening program. An existing twin pregnancy has to be checked for chorionicity because of the risk for twin to twin transfusion syndrome which can be treated if detected. Detection of chorionicity is possible only in the first trimester of pregnancy, a special qualification or training is not necessary. The project team considered the question as relevant and it was included as following PICO: accuracy of detection of chorionicity with ultrasound in the first trimester of pregnancy, gold standard is membrane check after delivery.

Detection of major malformations: A review with this topic is ongoing (IQWIG). For this review the question will not be answered twice. It was decided to exclude this PICO question.

Down syndrome was excluded due to already ongoing or existing reviews about this topic[9].

Currently the reimbursement of Down screening in Austria is based on the *humanogenetical contract (Humangenetikvertrag)* and includes amniocentesis (AC) or chorionic villus sampling (CVS) for women aged 35 or older at the beginning of pregnancy.

The frequency of AC and CVS is not documented now in a standardised way – data are not available for all regions of Austria.

Congenital heart diseases which are reported in literature as one major topic for ultrasound screening were not included into the PICO questions of this review because of their small prevalence in Austria. Therapeutic consequences after detection of heart failure can be set very early in the second trimester after more detailed organ screening. Adocumentation number exists in Austria for congenital surgery called *invasive prenataldiagnostic or therapeutic intervention* which was claimed 242 times in 2005 (199 in University Hospital Vienna, 22 in Hospital Linz, 21 in Hospital Wels[10]). Two surgeons of the Institute of Prenatal Medicine of the obstetrics and pediatric clinic in Linz[11] treat aortal stenoses, pulmonary valve atresiae, and hypoplastic left heart syndrome intrauterine with currently limited resources (about 10 cases). There is also existing evidence about the accuracy of first trimester ultrasound for detecting major congenital heart diseases[12].

The consequence of positive ultrasound for other chromosomal anomalies (Q99) is further testing by AC or CVS and if the diagnosis is ascertained to the termination of the pregnancy. Earlier termination is associated with lower risk for the pregnant woman.

Fetal loss rate after Standard AC is reported from 1,3% (Eiben 1997[13]) to 20,4% (Alfirevic 2003[14]). Fetal loss rate after CVS is reported from 6,3% to 27,4% (Alfirevic 2003). Fetal loss rate after early AC goes from 2% (Eiben 1997) to 6,8% (Cederholm 1997[15]). Interesting is a reported preterm birth rate of 32,4% after AC and 23,8% after CVS (Antsaklis 2002[16]). Repeated tests were necessary for AC in 5,2% and for 19% for early AC (Cederholm 1997).

Complications in abortion first versus second trimester of pregnancy[17] are shown in table 3.

Tab. 3

Study	Risk of abortion compl 1st trim	Risk of abortion compl 2nd trim	Definitions
Goodyear-Smith 2006[18]	1,5% (MOP)*; 0,6% (STOP)**		Compl. = hospitalization
Acharya 2004[19]	9,8%		Overall complication rate after ab in 1st trim
Bartlett 2004[20]	14.7 RR at 13-15 weeks of gestation (95% confidence interval [CI] 6.2, 34.7),	29.5 RR at 16-20 weeks (95% CI 12.9, 67.4), and 76.6 RR at or after 21 weeks (95% CI 32.5, 180.8).	0.7 per 100,000 legal induced abortions. The risk of death increased exponentially by 38% for each additional week of gestation
Johansen 2001[21]	8.7%		Hospital admission
Major 2000[22]	1%		Posttraumatic stress disorder
Khan 2006[23]	Abortion deaths were the highest in Latin America and the Caribbean (12%)		Maternal death
Al Taani 2005[24]		No major complications, no difference in side effects for MTOP versus STOP	

*medical terminations of pregnancy (MTOP)
**surgical terminations of pregnancy (STOP)

Increased risk of preterm birth and increased risk for gestational diabetes lead to more intensive observation during pregnancy.

The Calculation of gestational age are basic for further diagnostics in the second trimester and for the use of norm curves for biometric data.

After consideration of the draft questions based on the health insurance data and international literature the Peer Group (Dr. Gottfried Endel, Dr. Irmgard Schiller-Frühwirth, Mag. Ingrid Wilbacher) decided after discussions that the following objectives are the most relevant ones to be addressed in the planned review:

Determination of the accuracy of ultrasound investigation in the first pregnancy trimester (incl. 12th week) in diagnosing the following disorders:

- Other chromosomal anomalies **exclusive of** Down Syndrom (Chimäre 46,XX/46,XY, Chimäre 46,XX/46,XY with Hermaphroditismus verus, Hermaphroditismus verus with Karyotype 46,XX, Gonadendysgenesia, 46,XX with Streak-Gonades, 46,XY with Streak-Gonades, Fragile X-Chromosom, Syndrom of fragile X-Chromosom, ICD 10 Q99)
- Accuracy of detection of chorionicity with ultrasound in the first trimester of pregnancy, gold standard is membrane check after delivery
- Increased risk of preterm birth (ICD 10 P 07)
- Gestational diabetes
- Determination of gestational age

Determination of the outcomes after ultrasound investigation in the first pregnancy trimester (incl. 12th week) versus ultrasound investigation in the second and/or third trimester for the following target disorders:

- Other chromosomal anomalies **exclusive of** Down Syndrom (Chimäre 46,XX/46,XY, Chimäre 46,XX/46,XY with Hermaphroditismus verus, Hermaphroditismus verus with Karyotyp 46,XX, Gonadendysgenesia, 46,XX with Streak-Gonades, 46,XY with Streak-Gonades, Fragile X-Chromosom, Syndrom of fragile X-Chromosom, ICD 10 Q99)
- accuracy of detection of chorionicity with ultrasound in the first trimester of pregnancy, gold standard is membrane check after delivery
- Increased risk of preterm birth (ICD 10 P 07)
- Gestational diabetes
- Determination of gestational age

[1] S. Kahyaoglu, I. Turgay, M. Gocmen, N. Sut, and S. Batioglu. A new predictive scoring system including shock index for unruptured tubal pregnancy patients. *Eur.J.Obstet.Gynecol.Reprod.Biol.* 126 (1):99-103, 2006.
[2] M. Bloechle, H. Halle, and R. Bollmann. [Vaginal ultrasound cervix imaging in pregnancy—predictive value of suspicious findings on the subsequent course of pregnancy]. *Zentralbl.Gynakol.* 116 (12):697 705, 1994.
[3] H. Hoffmann, R. Chaoui, R. Bollmann, and A. Metzner. [Evaluation of the central hemodynamics of the fetus using pulsed Doppler ultrasound]. *Zentralbl.Gynakol.* 112 (11):673-678, 1990.
[4] T. Hitschold, E. Weiss, and P. Berle. [Doppler sonography of the umbilical artery, mode of delivery and perinatal morbidity in prolonged pregnancy]. *Z.Geburtshilfe Perinatol.* 192 (5):197-202, 1988.
[5] R. Sudik. [Results of an ultrasonic screening programme in the detection of intrauterine growth retardation]. *Z.Geburtshilfe Perinatol.* 186 (3):119-124, 1982.
[6]

Autor	**Publication Date**	**Pubmed ID**
O´Leary	2006	16582125
Kim	2006	16479057
Reddy	2006	16394055
Go	2005	16385832
Caughey	2006	16378329
De Biasio	2006	16378318
Maymon	2005	16238533
Hadlow	2005	16225579
Monni	2005	16158472
Coco	2005	16150267
Falcon	2005	16142826
Odibo	2005	16135588
Fuchs	2005	16104680
Wenstrom	2005	16104672
Bahado-Singh	2005	16104670
Viossat	2005	16012382
Rozenberg	2005	16005667
Avigdou	2005	15970804
Tran	2005	15914684
Spencer	2005	15906426
Zoppi	2005	15906408
Grant	2005	15894999
Vandecruys	2005	15880648
Cheng	2005	15863545
Dimitrova	2005	15853009
Orlandi	2005	15846188
Nicolaides	2005	15844559
Krampl	2005	15816021
Spencer	2005	15802030
Gianaroli	2005	15749067

[7]

Stover	16607591	fetal lung lesions
Salihu	16582122	small for gestational age as a risk of stillbirth
Tugrul	16440822	bacteriuria
Odibo	16378332	Kosteneffektivität des Screening aller Feten diabetischer Mütter mittels EKG
Miguelez	16374901	Labortests auf obstruktive Uropathie
Condous	16308901	ß HCG Messungen zur Feststellung von EUGs
Herman	16282229	Soziale Unterstützung schwangerer Afroamerikanerinnen mit geringem Einkommen
Davis	16183443	Uschall im Emergency room
	16026395	Plazentamagnetresonanz
Salomon	15909324	Wert der Wahl von Normwerttabellen
Longini	15890628	Labortest für fetale Wachstumsstörung
Dubiel	15841608	Laborwertanalyse
Muller	15791664	Labor
Theron	15762252	Gerätevergleich
Mavrou	15750009	Labor

[8]

Indication	Number of studies	Sensitivity	Specificity
Fetal growth reduction	3	32-60	83-92
Malformations	3	39-75	99-100
Heart diseases	3	70-93	45-99
Abnormities	5	65-92	66-100
Progostic of preterm birth	4	53-93	59-91
Preeclampsia	2	60-93	87-98
Umbilical blood flow and Outcome	1	77	67
Chorionicity of twins	1	100	97
Overweight	1	50	95
Ectopic pregnancy	1	100	100

[9] Scemana O, Préaubert-Hayes N, Rumeau-Pichon C. Evaluation of screening strategies for Down's Syndrome. *Public Health Guideline June* 2007. Economic Evaluation and Public Health Department.
[10] Sammel MEL 6743 *Invasiv pränataldiagnostischer oder – therapeutischer Eingriff* – Recherche in DIAG: 2005 199x im AHK Wien, 22x im LF+KKL Linz (K449) und 21x im KRSR KL Wels (K434) abgerechnet. Zahlen für 1. Halbjahr 2006 gleich.
[11] Institut für Pränatalmedizin an der Landes-Frauen- und Kinderklinik Linz (LFKK)
[12] Rasiah SV, Publicover M, Ewer AK, Khan KS, Kilby MD, Zamoras J. A systematic review of the accuracy of first-trimester ultrasound examination for detecting major congenital heart disease. *Ultrasound Obstet Gynecol* 2006;28:100-116.
[13] Fetal Diagn Ther. 1997 May-Jun;12(3):140-4.
On the complication risk of early amniocentesis versus standard amniocentesis.
Eiben B, Hammans W, Hansen S, Trawicki W, Osthelder B, Stelzer A, Jaspers KD, Goebel R.
Institut fur klinische Genetik und Frauenklinik, Evangelisches Krankenhaus
Oberhausen, Deutschland. eiben@cww.de
PMID: 9313070

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[14] Cochrane Database Syst Rev. 2003;(3):CD003252.
Amniocentesis and chorionic villus sampling for prenatal diagnosis.
Alfirevic Z, Sundberg K, Brigham S.
Department of Obstetrics and Gynaecology, University of Liverpool, Liverpool, UK, L69 3BX.
PMID: 12917956

[15] Prenat Diagn. 1997 Apr;17(4):311-7.
Comment in:
Prenat Diagn. 1998 Apr;18(4):405-7.
Prenat Diagn. 1998 Jan;18(1):87.
A prospective comparative study on transabdominal chorionic villus sampling and amniocentesis performed at 10-13 week's gestation.
Cederholm M, Axelsson O.
Department of Obstetrics and Gynaecology, Uppsala University, Sweden.
PMID: 9160382

[16] Ultrasound Obstet Gynecol. 2002 Nov;20(5):476-81.
Second-trimester amniocentesis vs. chorionic villus sampling for prenatal diagnosis in multiple gestations.
Antsaklis A, Souka AP, Daskalakis G, Kavalakis Y, Michalas S.
First Department of Obstetrics and Gynecology, Alexandra Maternity Hospital, University of Athens, Athens, Greece.
PMID: 12423485

[17] Search strategy 1

Search	Most Recent Queries	Time	Result
#22	Select **20** document(s)	05:35:10	20
#18	Search **((#13)) AND (#15)** Limits: **only items with abstracts, published in the last 10 years, Humans**	05:33:30	53
#16	Search **((#13)) AND (#15)**	05:25:51	181
#17	Search **((#14)) AND (#15)**	05:25:19	169
#15	Search **(((#8)) OR (#10)) OR (#12)**	05:24:20	897030
#14	Search **((#2)) AND (#6)**	05:23:41	1668
#13	Search **((#2)) AND (#4)**	05:23:21	1482
#12	Search **"Risk"[MeSH]**	05:22:52	461674
#10	Search **("Intraoperative Complications"[MeSH] OR "Postoperative Complications"[MeSH])**	05:21:37	318258
#8	Search **("Mortality"[MeSH] OR "Hospital Mortality"[MeSH] OR "Maternal Mortality"[MeSH])**	05:20:38	177487
#6	Search **"Pregnancy Trimester, Second"[MeSH]**	05:19:44	9210
#4	Search **"Pregnancy Trimester, First"[MeSH]**	05:19:14	9157

#2	Search **("Abortion, Induced"[MeSH] OR "Abortion, Therapeutic"[MeSH])**	03:42:02	27851

Search strategy 2

Search	Most Recent Queries	Time	Result
#7	Select **4** document(s)	06:20:04	4
#6	Search **((#3)) AND (#5)**	06:19:44	1066
#5	Search **"complications"[Subheading]**	05:42:25	1255702
#3	Search **"Abortion, Induced"[MeSH]**	05:41:49	27859
#1	Search **early versus late abortion**	05:40:59	26

Search strategy 3

Search	Most Recent Queries	Time	Result
#14	Select **12** document(s)	06:33:28	12
#13	Search **(((#6)) AND (#10)) AND (#12)**	06:33:04	41
#12	Search **"Gestational Age"[MeSH]**	06:29:13	50996
#10	Search **("Pregnancy Complications, Hematologic"[MeSH] OR "Pregnancy Complications, Neoplastic"[MeSH] OR "Pregnancy Complications, Infectious"[MeSH] OR "Pregnancy Complications, Cardiovascular"[MeSH] OR "Pregnancy Complications"[MeSH])**	06:28:40	254793
#7	Search **Endoxan**	06:26:38	38809
#6	Search **"Misoprostol"[MeSH]**	06:26:25	2270

[18] Aust N Z J Obstet Gynaecol. 2006 Jun;46(3):193-8.
First trimester medical termination of pregnancy: an alternative for New Zealand women.
Goodyear-Smith F, Knowles A, Masters J.
Auckland Medical Aid Centre, Mt. Eden, Auckland, New Zealand.
f.goodyear-smith@auckland.ac.nz
PMID: 16704471
[19] Eur J Obstet Gynecol Reprod Biol. 2004 May 10;114(1):69-74.
A randomized controlled trial comparing surgical termination of pregnancy with and without continuous ultrasound guidance.
Acharya G, Morgan H, Paramanantham L, Fernando R.
Department of Obstetrics and Gynaecology, The Whittington Hospital, London, UK. ganesh.acharya@unn.no
PMID: 15099874
[20] Obstet Gynecol. 2004 Apr;103(4):729-37.

Comment in:
Obstet Gynecol. 2004 Sep;104(3):635; author reply 636.
Risk factors for legal induced abortion-related mortality in the United States.
Bartlett LA, Berg CJ, Shulman HB, Zane SB, Green CA, Whitehead S, Atrash HK.
Maternal and Infant Health Branch, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Atlanta, Georgia 30341, USA. L.Barlett@CDC.gov
PMID: 15051566
[21] Ugeskr Laeger. 2001 Mar 12;163(11):1565-9.
[Legal abortion. An analysis of factors which can affect frequency of
complications]
[Article in Danish]
Johansen JK, Schmidt KL.
Centralsygehuset i Naestved, gynaekologisk/obstetrisk afdeling.
jctpj@mail.tele.dk
PMID: 11268811
[22] Arch Gen Psychiatry. 2000 Aug;57(8):777-84.
Comment in:
Arch Gen Psychiatry. 2000 Aug;57(8):785-6.
Psychological responses of women after first-trimester abortion.
Major B, Cozzarelli C, Cooper ML, Zubek J, Richards C, Wilhite M, Gramzow RH.
Department of Psychology, University of California, Santa Barbara, CA 93106. USA. major@psych.ucsb.edu
PMID: 10920466
[23] Lancet. 2006 Apr 1;367(9516):1066-74.
WHO analysis of causes of maternal death: a systematic review.
Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF.
Academic Department of Obstetrics and Gynaecology, University of Birmingham, Birmingham, UK.
PMID: 16581405

[24] East Mediterr Health J. 2005 Jul;11(4):657-62.
Termination of second trimester, complicated gestation.
Al-Taani MI.
Department of Obstetrics and Gynaecology, Queen Alia Military Hospital, Royal Medical Services, Amman, Jordan. maltaani@yahoo.com
PMID: 16700381