NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of fetal vesico-amniotic shunt for lower urinary tract outflow obstruction

Fetal lower urinary tract outflow obstruction prevents the unborn baby from passing urine. This can result in a reduction in the volume of amniotic fluid, and problems with the development of the baby's lungs and kidneys. A vesico–amniotic shunt is a tube that it is inserted into the unborn baby's bladder to drain the excess fluid into the surrounding space.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2006.

Procedure names

- Fetal vesico-amniotic shunt for bladder outflow obstruction.
- Fetal vesico-amniotic shunt for obstructive uropathy.
- Fetal vesico-amniotic drain.

Specialty societies

- British Association of Perinatal Medicine.
- British Maternal and Fetal Medicine Society.
- Royal College of Paediatrics and Child Health.
- Royal College of Obstetricians and Gynaecologists.

Description

Indications

Fetal lower urinary tract outflow obstruction. This condition may be associated with various developmental abnormalities. The obstruction may result from a number of pathologies including urethral atresia, or posterior urethral valves and can be partial or complete. Severe obstruction may lead to oligohydramnios (i.e. reduction in amniotic fluid volume) and both pulmonary and/or renal dysplasia. Pulmonary and/or renal dysplasia may be severe enough to cause death soon after birth from respiratory or renal failure respectively; or it may require ventilatory support and/or renal dialysis or kidney transplantation. The long-term prognosis for children who will require dialysis or transplantation in infancy is very poor.

Current treatment and alternatives

Alternative treatment options include: expectant management, termination of pregnancy, repeat vesicocenteses, or vesico-amniotic shunt

What the procedure involves

Fetal vescico-amniotic shunt for lower urinary tract outflow obstruction aims to decompress the obstructed fetal bladder and restore amniotic fluid dynamics and volume, thereby preventing oligohydramnios and pulmonary and/or renal hypoplasia. If vesico-amniotic shunt is considered, its timing is critical as it should ideally take place before the critical stages of lung and renal development have been completed. In some cases the fluid re-accumulates requiring repeated drainage procedures.

Fetal chromosomal analysis is usually performed before the procedure, to diagnose or exclude concomitant chromosomal abnormalities.

Under local anesthesia and ultrasound guidance, a metal cannula on a trochar is introduced though the mother's abdominal and uterine wall into the amniotic cavity and subsequently inserted into the bladder of the fetus. The trochar is removed and the drainage catheter inserted into the cannula and positioned with one end in the bladder and the other in the amniotic cavity. Different types of drainage tubes may be used including a double pigtail catheter. The cannula is then removed and the final position confirmed by ultrasound. The success of the procedure is determined by the absence of abnormal re-accumulation of urine in the bladder of the fetus on serial ultrasound scans. If the fluid re-accumulates, or the catheter dislodged, the procedure may be repeated.

Criteria for case selection for treatment by vesico-amniotic shunting are not well defined.

Efficacy

The evidence on efficacy relates to a meta-analysis of 7 controlled trials and 9 case series, and 5 individual case series studies.

Survival

A meta-analysis of 3 controlled trials comparing outcomes following vesico-amniotic shunting with no treatment found that there was a statistically significant improvement in perinatal survival in favour of shunting, Odds Ratio 2.53 (95 % confidence interval 1.08 to 5.93, p=0.03). This analysis was done excluding fetuses that were electively terminated. Postnatal survival for fetuses delivered alive (i.e. excluding in utero deaths and terminations) following shunting was better, although not significantly so, compared to no treatment, Odds Ratio 2.24 (95% confidence interval 0.89 to 5.59, p=0.09)[1]

Among case series reports survival following vesico-amniotic shunting ranged between 91% (21/23) at one year of follow up in one study[2], six out of eight in a second[3], 53% (8/15) in a third[4], and two out of five surviving into infancy in a fourth study[5].

Morbidity

Need for dialysis or transplantation

Among 18 infants surviving the neonatal period in one case series, 33% (6/18) of patients required dialysis or had renal transplantation[2]. A second case series study following up 8 survivors of vesico-amniotic shunting for between 1.5 and 5.5 years reported poor renal function in 2 children who required dialysis and or kidney transplant[4]. A third case series study of 6 surviving infants followed up for a mean period of 42 months reported that 2 infants required kidney transplantation[3]. Another case series study reported good renal function (defined as creatinine clearance of >70ml/min) in 45 % (8/18)[2] of infants followed up for a mean period of 5.8 years. Lastly another case series study reported good renal function (serum creatinine level of <1.0mg/dl) in six out of eight infants at one year follow-up[4].

Respiratory function

In one case series asthma was reported in 39% (7/18 of patients), and recurrent pulmonary infections in 28% (5/18)[2]. A second case series of 6 surviving infants reported that 2 infants required ventilatory support[3]. In one of the case series alluded to above, normal pulmonary function was reported in 55% (10/18) of infants[2].

Need for catheterisation / bladder voiding / recurrent urinary infections

Among 18 infants surviving the neonatal period in one case series, frequent urinary infections were reported in 50% (9/18) of patients, and 17% (3/18) had bladder dysfunction requiring catheterisation.

Quality of life

One case series including 18 children (out of a total of 23 fetuses originally included in the study) reported that the mean self-reported quality of life score (using the paediatric quality of life inventory 4.0) among infants who had been treated with a vesico-amniotic shunt was 84.19 points at 5.8 years follow up, which compares well with a score of 83.0 points in a healthy infant population[2].

Safety

The evidence on safety relates to 5 case series studies.

Prenatal complications

The most commonly reported complication across the studies reviewed is shunt displacement. This was reported to have occurred in between 2 of 9, 28% (5/18)[2], and 60% (9/15)[4] of fetuses, often requiring replacement shunt placement.

One case series reported that premature rupture of membranes occurred in 6% (1/18) fetuses 4 days after the placement of the shunt[2].

Post-natal complications

There was one report each of bladder prolapse at birth, and requirement for intermittent catheterisation.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to fetal vesico-amniotic shunt for lower urinary tract outflow obstruction. Searches were conducted via the following databases, covering the period from their commencement to 28 March 2006: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. If these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with bladder outflow obstruction.
Intervention/test	Vesico-amniotic shunt.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on one meta-analysis and 5 case series

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in appendix A.

Existing reviews on this procedure

There was one meta-analysis relating to this procedure, which is described in table 2.

Related NICE guidance

There is no other NICE guidance related to this procedure.

Table 2 Summary of key efficacy and safety findings on fetal vesico-amniotic shunt for lower urinary tract outflow obstruction

Abbreviations used: OR – odds ratio, CI – confidence interval,			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
Clark T J (2003)[1] **Meta analysis of controlled trials and case series** UK Study periods: Not stated **n= 342 cases in all studies included, with 76 drainage procedures (71 vesico-amniotic shunts) for pooled data analysis from 4 controlled trials.** Population: Mean age not stated for each primary study. Extensive literature searches carried out to the end of 2002. In total 9 case series (147 fetuses) and seven controlled trial (195 fetuses) (total number of active and control cases not defined) Fetuses with ultrasonic evidence of lower urinary tract obstruction. Predicted fetal prognosis, based on gestational age, underlying pathology, renal damage, amniotic fluid volume, bladder refilling characteristics, and urinary biochemistry, varies both within and between primary studies included. Intervention: vesico-amniotic shunt or open fetal bladder surgery Vs vesicocentesis alone. Most cases that underwent vesico-amniotic shunting had previously received a vesicocentis. **Mean follow-up: Not stated for each primary study** Disclosure of interest: Not stated	**Fetal survival** Of the 106 vesico-amiotic shunts included in nine case series, the overall fetal loss rate ranged from 0% to 100%. There was a statistically significant improvement in fetal survival (excluding termination of pregnancy) with intervention compared to no intervention. OR 2.53 (95% CI 1.08 to 5.93) (p=0.03) Also, there was a statistically significant improvement in fetal survival (including voluntary termination of pregnancy) with drainage compared to no intervention. OR 4.24 (95% CI 2.10 to 8.58) (p<0.001) **Postnatal survival** Excluding fetuses that died in utero or were electively terminated, there was an improvement in post natal survival with drainage compared to no treatment, although this difference was not statistically significant. OR 2.24 (95% CI 0.89 to 5.59) (p=0.09). Fetuses with poor predicted prognosis at the time of intervention appear to benefit most from drainage, in subgroup analysis of two studies where this comparison was possible.	None reported. Inadequate description of the surgical intervention and variation in outcomes reported in primary studies meant that failure rates and complications of vesico-amniotic shunts could not be calculated.	Study selection performed by two independent researchers York Centre for Reviews and Dissemination criteria used to assess study methodological quality characteristics for inclusion. Primary studies used different criteria for case selection, employed different techniques for the procedure (including different shunting procedures and some cases of open fetal surgery), and different outcome measures. So there may be clinical heterogeneity between pooled studies. Statistical heterogeneity between studies was calculated with the Chi-squared test, and the results was not significant, however, this test has low power to determine heterogeneity when a low number of studies are pooled. Studies were pooled using a fixed-effects model to calculate the Peto Odds ratio intervention versus no treatment. Meta analysis of observational data can produce spurious results as a consequence of confounding or selection bias.

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
Baird J-M (2005)[2] **Case series** USA – 2 centres Study period: not stated **n=23 (18 completed outcomes assessment)** Population: Mean gestational age at diagnosis = 19.4 weeks, gestational age at shunting = 21.9 weeks. Good prognosis = 72%, borderline prognosis = 11%, poor prognosis = 17%. Male = 100%. The mean gestational age at delivery was 34.6 weeks, and birth weight 2.57 Kg. Indications: Fetuses with clear evidence of bladder outflow obstruction and oligohydramnios, grouped in terms of prognosis based on prior vesicocentesis into good, borderline and poor. Technique: No details provided. **Mean follow-up = 5.8 years (for 18 survivors)** Disclosure of interest: Primary author received research grants from two foundations, not clear if any commercial interests were represented.	**Post natal mortality** There were two neo-natal deaths from pulmonary hypoplasia (one had good and one poor prenatal prognosis). First year survival rate was 91% (21/23). Long term efficacy (at a mean follow-up of 5.8 years, for 18 out of 23 survivors) **Growth:** 17% (3/18) of children were <5th centiles for both height and weight. **Respiratory function:** Normal pulmonary function was achieved in 55% (10/18) of infants, and acceptable renal function (creatinine clearance of >70ml/min) was seen in 45% (8/18). Renal Renal transplant 33% (6/18) Mild renal insufficiency 22% (4/18) Dialysis 33% (6/18) Respiratory Asthma 39% (7/18) Recurrent pulmonary infections 28% (5/18) Sleep apnoea 11% (2/18) **Bladder function and urinary infections:** Spontaneous voiding was achieved in 61% (11/18) of infants, and 33% (6/18) had no urinary infections. **Quality of life:** The Paediatric quality of life inventory PedsQL 4.0 scales was used to assesses quality of life both by child (where able to complete the form) and parents. Overall scores were 79.16 points (± 12.34) from the parents of 13 children who completed the questionnaire. This compares with 87.61 points for a healthy population, and 74.22 points in chronically ill children, based on results from another study. The overall child self-reported score was 84.19 points (± 12.84), which compare with 83.0 points in a healthy population and 77.19 points in chronically ill children.	**Prenatal complications** Overall, complications after shunting occurred in 44% (8/18) of fetuses. Complication Rate (n=18) Shunt displacement 28% (5/18) Premature rupture of membranes 6% (1/18) **Postnatal complications** Complication Rate (n=18) Abdominal omental herniation 11% (2/18) Special diet required 55% (10/18) Musculoskeletal Abdominal muscle insufficiency 22% (4/18) Mild scoliosis 11% (2/18) Pectus excavatum 22% (4/18) Bladder Combined spontaneous voiding and catheterisation 17% (3/18) Catheterisation 17% (3/18) Vesicostomy 6% (1/18) Urinary infections Occasional infections 17% (3/18) Frequent infections 50% (9/18) Prophylactic antibiotics 66% (12/18) Neurological issues Learning disabilities 11% (2/18) Speech therapy 17% (3/18) Physical therapy 17% (3/18) Associated abnormalities Cryptorchidism 50% (9/18) Inguinal hernias 17% (3/18)	Safety and long term efficacy outcomes are only analysed in surviving infants. There is potential for selection bias: Of 31 fetuses originally identified where shunting was undertaken 26% (8/31) were lost to follow up, and 10% (3/31) of parents refused to participate or did not return outcome questionnaires. The experience of clinicians undertaking the shunt placement is not stated. Outcomes are reported separately for different aetiologies of bladder outflow obstruction, established post-natally (posterior urethral valves, urethral atresia, prune belly syndrome) but not extracted here. Not reported whether renal replacement therapy requirement (dialysis) affected quality of life scores.

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
Johnson M P (1994)[4] **Case series** USA Study period: not stated **n=15** Population: Gestational age at diagnosis from 14 to 24 weeks. Fetal karyotyping undertaken and only male fetuses were considered for shunting. Indications: Cases with bladder outlet obstruction assessed ultrasonographically, and decreased amniotic fluid volume were included in the study. Technique: Vesico-amniotic shunting by placement of a double pig-tailed shunt under continuous ultrasonic guidance. **Follow-up = between 1.5 and 5.5 years** Disclosure of interest: not stated.	**Survival** Of the 15 cases shunted 47% (7/15) died in utero or neonatally. Of those who died, 3 had predicted good prognosis (based on fetal urine samples and progressive improvement after repeated drainage), and 4 were determined to have a poor prognosis. **Renal function** Of the 8 survivors good renal function (serum creatinine level at one year of ≤1.0 mg/dl) was reported in 6 infants. Poor renal function requiring dialysis and awaiting transplant was reported in 2 of 8 infants	**Prenatal complications** Complication — Rate (n=15) Shunt displacement into the amniotic space — 40% (6/15) Shunt displacement intraperitoneally, resulting in urinary ascites — 20% (3/15)	A mixture of prospectively identified (n=28) and retrospectively reviewed cases (n=6) for case accrual In eight fetuses that were followed up without shunting, three obstructions resolved after initial vesicocenticies. Four resulted in intrauterine death, and one neonatal death due to pulmonary hypoplasia. It is not clear why these cases were not treated. Authors state the importance of serial vesicocentises and subsequent improvement in urine values before shunting. Authors suggest that fetuses that should be excluded from treatment include those with congenital abnormalities, female or those with chromosomal abnormalities, those with small for age kidneys, and those with renal cortical cysts. One fetus treated was one of twins. Authors state that fetal deaths occurred following an interval of at least one week after the shunt placement.

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
McLorie G (2001)[3] **Case series** Canada Study period: 1989 and 1998 **n=9** Population: Fetuses of between 20 and 28 weeks of gestation Indications: Bilateral hydronephorsis with bladder outflow obstruction, oligohydramnios, and a decrease in fetal urine hypertonicity. Technique: Following pre-procedural assessment of renal function by diagnostic bladder taps, shunting performed with a double pigtail catheter placed in the bladder and amniotic cavity. **Mean follow-up = 42 months** Disclosure of interest: Not stated	**Pre-natal outcomes** No incidents of preterm labour or chorioamnionitis reported. Bladders were successfully drained in 100% (9/9) of cases. Amniotic fluid was restored to 89% (8/9) of fetuses. 100% (8/8) of fetuses were delivered following at least 30 weeks gestation (one parent elected termination following shunt insertion). **Post natal outcomes** Death: Two of eight neonates (25%) who were treated with a shunt died shortly after birth from severe restrictive pulmonary disease. Renal function: Two of the surviving six (out of eight) neonates required kidney transplantation. Normal renal function (creatinine clearance of >70ml/min) was seen in 50% (3/6) infants, and 83% (5/6) of infants were voiding freely. Respiratory function: Two of the surviving six (out of eight) neonates required ventilatory support.	**Pre-natal complications** Complication – Rate (n=9) Shunt dislodgement requiring repeat insertion procedure – 22% (2/9) **Post natal complications** Complication – Rate (n=6) Bladder prolapse at birth requiring emergency vesicostomy – 17% (1/6) Requirement for intermittent catheterisation – 17% (1/6)	Retrospective study of consecutive cases. Indications for shunting were present in 13% (12/ 89) fetuses with bladder outflow obstruction. Shunting was accepted by 9 out of 12 parents. Authors state that accurate diagnosis of obstruction with bladder distension, and oligohydramnios is a prerequisite for consideration of shunt treatment. All surviving patients underwent some form of postnatal treatment (pyelostomy or vesicostomy) The experience of clinicians undertaking the shunt placement is not stated. The outcome for one fetus with bladder outlet obstruction where no shunt was inserted (parental choice) was stillbirth.

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
Shimada K (1998)[6] **Case series** Japan Study period: not stated **n=6 (5 had vesico-amniotic shunting, 1 had an open pyelo-amniotic shunt)** Population: Mean gestational age at diagnosis 18 weeks, Male = 67%, Prune belly syndrome =50%. Gestational age at delivery 31 to 37 weeks. Indications: 4 fetuses had experienced a decrease in amniotic fluid volume. Technique: Patients underwent shunting and, after birth, received neonatal respiratory and circulatory care. Infants surviving the neo-natal period were referred for specialist urological management. **Mean follow-up range 4 to 60 months** Disclosure of interest: Not stated.	**Pre-natal outcomes** None reported **Post-natal outcomes** Respiratory function: Good long term pulmonary function was achieved in 4 of 6 infants. <u>Respiratory</u> Frequent infections 33% (2/6) Intermittent home oxygen support. 17% (1/6) Renal function: 2 of 6 infants had a solitary functioning kidney. A nadir creatinine clearance level of <0.4 mg/dl was reported in 5 of 6 infants during their first year of life.	**Complications** All complications reported relate to the post neo-natal period (not defined) <u>Urological</u> Rate (n=5) Antegrade valve ablation for posterior urethral valves 20% (1/5) Recurrent urinary tract infection requiring antireflux surgery 60% (3/5) Hypoplastic urethra 100% (5/5) Intermittent catheterisation with inadequate detrusor muscle activity 100% (5/5)	No details are available with regard to survival following shunting, it is not stated what fraction of the fetuses treated these 6 cases represent. Therefore there is an unknown potential for selection bias. Separate reporting for the 5 fetuses who received vesico-amniotic shunting only for some of the examined outcomes The cases were transferred to the study institution from 4 sites, it is not clear how much experience of shunt placement each centre may have had. The severity and aetiology of urological abnormality varies between cases. Four neonates required ventilatory support.

Abbreviations used: OR – odds ratio, CI – confidence interval,

Study details	Key efficacy findings	Key safety findings	Comments
Makino Y (2000)[5] **Case series** Japan Study period: 1995 to 1998 **n=5** Population: Mean gestational age at diagnosis = 20.8 weeks, mean gestational age at shunting = 24.2 weeks, prune belly syndrome n=2, cloacal anomaly n=1, urethral stenosis n=1, sacrococcygeal teratoma n=1. The mean gestational age at delivery was 30.6 weeks, and weight was 1.958 Kg. Indications: Fetuses without chromosomal defects, with oligohydramnios, and good renal function as defined by urinalysis. Technique: Following serial vesicocenteses, a double basket catheter was inserted under ultrasound guidance. **Follow-up = 18 to 48 months** Disclosure of interest: Not stated	**Survival** Of the 5 fetuses treated 1 died in utero at 19 weeks gestation (hydrops present, and tight cord coiling around the neck), 2 died in the neonatal period (at 2 and 7 hours), and 2 survived into infancy.	**Complications** In one 4 year old infant with cloacal anomaly there was psychomotor developmental delay, and signs of clonic convulsions. In a patient with prune belly syndrome there was psychomotor developmental delay and hydrocephalus at final follow up at 18 months.	Not stated whether the cases are sequential, or selected. Authors state that earlier placement of shunts (before 20 weeks) may have avoided hypoplasia Authors state that greater standardisation is required for patient selection Expected prognosis at baseline was defined for each fetus but not discussed in results.

Validity and generalisability of the studies

- Some studies report outcomes with the denominator of fetuses treated, and some based on survivors only.
- Some studies describe different aetiologies of bladder outflow obstruction, but do not report outcomes based on these subgroups.

Specialist Advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr B Martin, Prof. M Kilby, Mr K Hinshaw, Dr S Cooper, Mr G Mason

- All advisors considered this to be an established procedure.
- The intended benefits of shunting are live birth, with preserved renal function and avoidance of pulmonary hypoplasia
- Reported and anecdotal adverse events include preterm labour, shunt blockage or displacement leading to failure to drain the bladder, fetal trauma, and babies born with end stage renal failure
- Additional theoretical complications include fetal hydrops, urinary ascites, trauma to maternal organs, and maternal infection.
- Practitioners need to be skilled in ultrasonic guided surgery, and high quality equipment is required.
- There is an ongoing trial at Birmingham recruiting 200 fetuses for a randomised controlled trial comparing shunting to conservative management.
- There is some controversy over the type and size of shunt to use.

Issues for consideration by IPAC

- Uncertainties remain as to the effectiveness of the procedure particularly in its ability to prevent renal damage.
- If dialysis is required in the first few months of life, 80% die before transplantation. If a patient is subsequently transplanted as a young child, a new transplant is usually required by the age of 10. Many such children develop malignancy by their 18th birthday.
- Efficacy outcomes may, at least in part, be influenced by presence or absence of underlying concomitant conditions and, therefore case selection is important.
- The prognosis for fetuses without intervention is poor.
- Fetuses may have concomitant genetic defects that may not be evident at the time of diagnosis of lower urinary tract outflow obstruction.

References

1 Clark TJ, Martin WL, Divakaran TG et al. (2003) Prenatal bladder drainage in the management of fetal lower urinary tract obstruction: a systematic review and meta-analysis. [Review] [36 refs]. *Obstetrics & Gynecology* 102: 367-382.

2 Biard JM, Johnson MP, Carr MC et al. (2005) Long-term outcomes in children treated by prenatal vesicoamniotic shunting for lower urinary tract obstruction. *Obstetrics & Gynecology* 106: 503-508.

3 McLorie G, Farhat W, Khoury A et al. (2001) Outcome analysis of vesicoamniotic shunting in a comprehensive population. *Journal of Urology* 166: 1036-1040.

4 Johnson MP, Bukowski TP, Reitleman C et al. (1994) In utero surgical treatment of fetal obstructive uropathy: a new comprehensive approach to identify appropriate candidates for vesicoamniotic shunt therapy. *American Journal of Obstetrics & Gynecology* 170: 1770-1776.

5 Makino Y, Kobayashi H, Kyono K et al. (2000) Clinical results of fetal obstructive uropathy treated by vesicoamniotic shunting. *Urology* 55: 118-122.

6 Shimada K, Hosokawa S, Tohda A et al. (1998) Follow-up of children after fetal treatment for obstructive uropathy. *International Journal of Urology* 5: 312-316.

Appendix A: Additional papers on fetal vesico-amniotic shunt for lower urinary tract outflow obstruction not included in table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (Table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Austin JC, Canning DA, Johnson MP, Flake AW, Carr MC. Vesicoamniotic shunt in a female fetus with the prune belly syndrome. Journal of Urology 2001; 166(6):2382.	Case report n=1 FU=?	Female fetus with prune belly syndrome, delivery by caesarean at 39 weeks	Case series are included in table 2
Chan FY, Borzi P, Cincotta R, Burke J, Tudehope D. Limb constriction as a complication of intra-uterine vesico-amniotic shunt: fetoscopic release. Fetal Diagnosis & Therapy 2002; 17(5):315-320.	Case report n=1 FU=2 years	Case of catheter end wrapping round the left thigh	Case series are included in table 2
Freedman AL, Johnson MP, Smith CA, Gonzalez R, Evans MI. Long-term outcome in children after antenatal intervention for obstructive uropathies.[see comment]. Lancet 1999; 354(9176):374-377	Case series n=34 FU=2 years	13 deaths and 21 survivors	Potential the same cases as in Clarke (2003)
Gehring JE, Cain MP, Casale AJ, Kaefer M, Rink RC. Abdominal wall hernia: an uncommon complication of in utero vesicoamniotic shunt placement. Urology 2000; 56(2):330.	Case report n=3 FU=to delivey	All 3 cases had good pulmonary development, 2 had renal failure requiring dialysis.	Case series are included in table 2
Irwin BH, Vane DW. Complications of intrauterine intervention for treatment of fetal obstructive uropathy. Urology 2000; 55(5):774.	Case report n=1 FU=?	Dislodgement of initial shunt and failure of replacement shunt	Case series are included in table 2

Jung E, Won H-S, Shim J-Y, Lee PR, Kim A, Kim KS. Successful outcome following prenatal intervention in a female fetus with bladder outlet obstruction. Prenatal Diagnosis 2005; 25(12):1107-1110.	Case report n=1 FU=12 months	Female fetus with a successful outcome	Case series are included in table 2
Kim SK, Won HS, Shim JY, Kim KS, Lee PR, Kim A. Successful vesicoamniotic shunting of posterior urethral valves in the first trimester of pregnancy. Ultrasound in Obstetrics & Gynecology 2005; 26(6):666-668	Case report n=1 FU=36 months	Child survived and has normal renal function at 3 years of age	Case series are included in table 2
Kuga T, Esato K, Sase M, Nakata M, Kaneko J, Inoue T. Prune belly syndrome with penile and urethral agenesis: report of a case. Journal of Pediatric Surgery 1998; 33(12):1825-1828.	Case report n=1 FU=4 weeks	Baby born at 33 weeks, and cystostomy performed	Case series are included in table 2
Manning FA, Harman CR, Lange IR, Brown R, Decter A, MacDonald N. Antepartum chronic fetal vesicoamniotic shunts for obstructive uropathy: A report of two cases. American Journal of Obstetrics & Gynecology 1983; 145(7):819-822.	Case report n=2 FU=6 months	One fetus died in the neonatal period with pulmonary hypoplasia, one alive and healthy	Case series are included in table 2
Perez-Brayfield MR, Gatti J, Berkman S, Eller D, Broecker B, Massad C et al. In utero intervention in a patient with prune-belly syndrome and severe urethral hypoplasia. Urology 2001; 57(6):1178.	Case report n=1 FU=to delivey	Survival to delivery at 36 weeks good preservation of renal and respiratory function	Case series are included in table 2
Robichaux AG, III, Mandell J, Greene MF, Benacerraf BR, Evans MI. Fetal abdominal wall defect: a new complication of vesicoamniotic shunting. Fetal Diagnosis & Therapy 1991; 6(1-2):11-13.	Case report n=2 FU=to delivery	Two cases of fetal abdominal wall defect following shunting	Case series are included in table 2
Szaflik K, Kozarzewski M, Adamczewski D. Fetal bladder catheterization in severe obstructive uropathy before the 24th week of pregnancy. Fetal Diagnosis & Therapy 1998; 13(3):133-135.	Case series n=5 FU=?	1 baby died of respiratory distress syndrome 4 others survived	Larger case series are included in table 2
Tanemura M, Suzumori K. Prune-belly syndrome treated with vesicoamniotic shunting at 17 weeks of gestation: Report of a case. Journal of Medical Ultrasound 2000; 8(4):257-261.	Case report n=1 FU=2 days	Successful fluid reduction	Case series are included in table 2

Appendix B: Related published NICE guidance for fetal vesico-amniotic shunt for lower urinary tract outflow obstruction

Guidance programme	Recommendation
Interventional procedures	None applicable
Technology appraisals	None applicable
Clinical guidelines	None applicable
Public health	None applicable

Appendix C: Literature search for fetal vesico-amniotic shunt for lower urinary tract outflow obstruction

IP: 332 vesicoamniotic shunt		
Database	**Date searched**	**Version searched**
Cochrane Library	28.3.06	2006 Issue 1
CRD databases	"	-
Embase	"	1980–2006 week 12
Medline	"	1966–March week 3 2006
Premedline	"	1966–present
CINAHL	"	1982–March week 4 2006
British Library Inside Conferences	"	-
NRR	"	2006 Issue 1
Controlled Trials Registry	"	-

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

1 vesico amniotic.tw.
2 vesicoamniotic.tw.
3 bladder drain$.tw.
4 (pigtail adj (catheter$ or shunt$)).tw.
5 (drain$ adj2 (catheter$ or shunt$)).tw.
6 Urinary Diversion/
7 Urologic Surgical Procedures/
8 or/1-7
9 exp Urethral Obstruction/
10 lower urinary tract obstruction$.tw.
11 obstructive uropathy.tw.
12 (bladder adj (outflow or outlet) adj obstruct$).tw.
13 Hydronephrosis/
14 hydronephrosis.tw.
15 urethral hypoplasia.tw.
16 or/9-15
17 8 and 16
18 (fet$ or foet$ or utero$ or inutero$ or intrauterine).tw.
19 (antenatal$ or prenatal$).tw.
20 fetal diseases/su
21 Fetus/su [Surgery]
22 or/18-21
23 17 and 22