	Vasa Praevia and Placenta Praevia Screening **1 November 2008** **(a)Review of the Evidence for Screening for Vasa Praevia (Previa) against NSC criteria**	**Response and comments by;** **VASA PRAEVIA** **raising awareness** www.vasapraevia.co.uk Registered Charity No. 1109893
	The Condition	
	1 Importance of Health Problem	
	The main aim of antenatal screening for vasa praevia is to prevent perinatal deaths.	It is extremely important to establish whether the antenatal screening referred to herein relates to routine antenatal screening for all pregnant women at 20 weeks or whether, knowing of risk groups and other associated risk factors, the screening referred to is "routine" antenatal screening for those in the known risk groups either at 20 weeks and/or again at 32 – 36 weeks. This review is not clear in this regard.
	Vasa praevia is a recognised cause of fetal intrapartum death first recognised clinically and reported upon in 1801. There is a high fetal mortality associated with rupture of the vasa praevia, with death resulting from rapid and catastrophic fetal exsanguination. Early detection is desirable as planned caesarean section can circumvent the risks.	
	The prevalence of vasa praevia has been variously reported as 1.5-4:10,000 births [1, 2].	NB. This does not include most recent published study and the stated prevalence therein of 1:1,340 - Baulies S, Maiz N, Munoz A, et al. Prenatal ultrasound diagnosis of vasa praevia and analysis of risk factors. Prenatal Diagnosis - 2007; 27:595-599. Nor does it include details or statistics from the forthcoming QCCH audit 2008, referred to the NSC by Elizabeth Daly Jones et al..
	The total number of live births for England and Wales in 2006 was 669,601 (621,589 in England) with an additional 3602 stillbirths resulting in an overall number of 673,203	NB. Why do these figures not include Scotland or NI? Also NB. If the prevalence of vasa praevia is as high

	registered births[3]. Using the quoted prevalence range, the anticipated number of cases would be to the order of up to 269 cases per annum.	as 1:1,340 (Baulies et al 2007 - *supra*) the anticipated number of cases could be 502 per annum (England & Wales only). However assuming only a 10% increase in the total UK birth rate when including births from Scotland & NI, this would give an anticipated number of cases annually of 552 in the UK. This is an important issue as currently this review may misstate the position by over 50% and thus under represent the huge social as well as public health issue being dealt with here.
	Until recently vasa praevia has been considered to be difficult to diagnose and has not been specifically looked for. It is not a common condition. In addition the diagnosis can be missed in cases of sudden intrapartum death, or the diagnosis can be delayed, thereby compromising an accurate estimation of prevalence.	NB. The first sentence is agreed and also serves as a clear acceptance that vasa praevia is no longer considered difficult to diagnose. The final sentence is also very important because there is currently no reliable source of national data either in the UK or elsewhere which consistently records the frequency or occurrence of the condition vasa praevia. Indeed experience has shown (and ONS data suggests) that even following a pathological examination of the placenta after the rupture of a previously undiagnosed case of vasa praevia where a neonatal death or stillbirth has occurred, the description of vasa praevia is often not used by medical professionals as a cause of death on death certificates. Too often the generic ante partum haemorrhage (APH) is used – wholly masking the true prevalence of the condition. Indeed another common mis-description on death certificates is placental abruption. This is a very important issue as it has undoubtedly led to the massive underreporting and thus importance of the of the condition (i.e. ONS statistics revealed that in 2005 there were zero deaths due to vasa praevia – which of course is a nonsense and demonstrates the problem of the over reliance on such official figures when addressing this important public health and social issue).
	The neonatal deaths referred to as being due to vasa praevia on death certificates in	Agreed.

	England and Wales between 2001 and 2005 are almost certainly unreliable and reflect a marked underrepresentation.	
	Given these circumstances the prevalence is probably more along the lines of 4:10,000 rather than 1.5:10,000 births.	Sadly this represents no more than guesswork on the part of the author – however, even anecdotally it is evident that vasa praevia occurs with a far greater prevalence than 1.5:10,000. VPRA query why the author has left out of this computation of the purported prevalence the most recent published study; Baulies S, Maiz N, Munoz A, et al. Prenatal ultrasound diagnosis of vasa praevia and analysis of risk factors. Prenatal Diagnosis - 2007; 27:595-599, this study quotes a prevalence of 1:1,340.
	The difficulty in establishing the diagnosis easily after birth limits the study of sensitivity and specificity of prenatal screening and diagnosis.	We are surprised at this statement because we do not believe that a velamentous insertion of the umbilical cord is difficult to establish on a gross examination of the placenta after birth. It is VPRA's view that in a case involving a previously undiagnosed vasa praevia, such findings on gross examination when coupled with the existence of pre-birth fetal distress and the probable exsanguination of the fetus - would lead a moderately aware obstetric team to have no such difficulty in establishing the diagnosis. Accordingly VPRA can see no such limit on the study of sensitivity and/or specificity of any prenatal diagnosis. Furthermore in cases diagnosed by ultrasound antenatally there should be little difficulty in securing the placenta for pathological examination or even gross examination to confirm the diagnosis. [see generally Sepulveda et al; Ultrasound Obstet. Gynecol. 2003;21:564-569 at 568.]
	2(i) Epidemiology	
	The condition known as vasa praevia occurs when fetal vessels cross or run within the membranes between the amnion and chorion in close proximity to the internal cervical os. These vessels are unprotected by Wharton's jelly and are at risk of rupture when the fetal membranes rupture (spontaneously or artificially) resulting in an	

	acute and severe fetal haemorrhage. Haemorrhage can also occur prior to rupture of the membranes.	
	The two main types of vasa praevia are:- (a) when the umbilical cord inserts directly into the membranes rather than the placenta (a velamentous insertion) (Type I) and (b) when there is as an additional separate (succenturiate) placental lobe with vessels crossing over from one portion of the placenta to the other (Type II)[4,5].	
	However multi-lobed placentas and velamentous insertion are seen in approximately just 1% of singleton pregnancies[6].	
	In addition only approximately 2% (1:50) of velamentous insertions are associated with vasa praevia[7].	
	In the vast majority (99%) of singleton pregnancies the umbilical cord will insert either directly into the placental tissue or marginally on the placental edge.	Marginal insertion of the umbilical cord also presents a risk for vasa praevia - a vessel that courses over the edge of marginal placenta or placenta praevia may become a vasa praevia after the extension of the placenta to a better vascularised area (i.e. where the placenta later "recedes"). This is where RCOG Greentop Guideline No 27 needs revision at the very least.
	The condition is seen more commonly in *multiple pregnancies* which account for approximately 10% of the cases[8]. Conditions such as *placenta praevia* and *multi-lobed/bi-lobed/succenturiate placentas* are also associated with an increased risk of vasa previa. Differential growth between the placenta and lower uterus during advancing pregnancy can reveal vasa praevia in cases where the placental edges initially covered the internal cervical os, so that prior ultrasonic evidence of a placental edge over the internal os represents an important risk factor for women with suspected vasa praevia. There is a highly significant association between vasa praevia at delivery and a history of second-trimester placenta praevia[9]. *In vitro fertilisation*	It is important not to overlook pregnancies that start as a multiple pregnancy but result in a singleton – such as a failed twin in an IVF conception. This paragraph also deals with a vitally important point, because the vast majority of those who contact VPRA, (usually with a missed diagnosis of vasa praevia), have in fact been earlier diagnosed with placenta praevia, and following their 32 week follow up scan, which invariably reveals that the leading edge of the placenta has receded - they are then advised to have a vaginal delivery - with terrible consequences as the sonographer has not excluded the underlying vasa praevia. The NSC can ensure that the revision of RCOG Greentop Guideline No. 27 takes account of these cases, and the NSC cannot fail to act on this now,

	increases the risk of vasa praevia to 1:300[10] for reasons that are unclear. However given that vasa praevia is thought to be caused by a disturbed orientation of the blastocyst at implantation, it is probably related to the IVF embryo transfer procedure. Cases of fetal exsanguination and death will nonetheless occur in the absence of any risk factors[11], prompting calls for a systematic assessment of the placental cord insertion during routine second trimester obstetric ultrasound.	given the review in hand. It would be bordering on clinical negligence if clinicians did not attempt to exclude vasa praevia in all cases where there has been an earlier diagnosis of placenta praevia – and this review provides the perfect opportunity to address the failings in the current system. Indeed what is the difficulty in applying colour Doppler over the os at this stage, even where it is clear that the placenta praevia has receded? [Whilst this clearly represents a suggestion for selective screening of placenta praevia cases – it is not a concession that screening should not be for all pregnant women. The reason for this suggestion is because there is already a protocol to screen for placenta praevia at 32 weeks and given there is an odds ratio of 22.86 of vasa praevia occurring in a second trimester placenta praevia case (Baulies et al – *supra*) – it would be negligent not to recognise this risk and act upon it]. Furthermore in 2005 there were in the region of 38,000 IVF pregnancies in the UK. This would potentially account for approximately 127 vasa praevia cases per annum - on any view this is a staggering proportion of the guesstimated number of cases. It is VPRA's view that it is highly questionable on ethical grounds for parents to be, who have conceived by IVF and thus invested hugely in both a physical and an emotional context - not to mention financially - to not be made aware of the increased risk of vasa praevia. Given such information - this would provide the choice for these parents ultimately to opt for screening. Given the huge investment of public funds into IVF treatment (NHS), it is in the public interest that this funding is not wasted in cases by a failure to diagnose vasa praevia. It should also be noted that cases of fetal exsanguination and death will inevitably also occur notwithstanding the implementation of any routine screening program - whether or not risk factors have prompted screening - this will occur even in cases where there has been an antenatal diagnosis – as this is true of any diagnostic process.
	Until recently international coding has	This will only be effective if physicians use it

	shared vasa praevia and velamentous insertion so that medical discharge code scanning has been unreliable; the most recent version of the International Classification of Diseases (10th) now has a separate code for vasa praevia (0.69.4).	properly, rather than opt for the shorthand APH. It will prove very useful if the NSC recommends and sponsors data collection on vasa praevia by UKOSS, or funds research into the condition. However awareness of vasa praevia as a condition will need to be raised enormously amongst midwives, obstetric and paediatric staff, and whilst VPRA have done a lot to raise the awareness of the condition we have not seen any real evidence of the raising of awareness by those properly responsible for this task.
	2(ii) Natural History	
	The diagnosis of vasa praevia is usually only made after the fetal haemorrhage has occurred. Without serious fetal bleeding the diagnosis cannot often be made. In the absence of antenatal recognition the typical picture is that of ruptured membranes, painless vaginal bleeding and acute fetal distress or death. Vasa previa often remains unsuspected until then. Velamentous insertion of the cord has also been associated with other adverse pregnancy outcomes.	As things stand this has been the position for the last 100 years. With regard to the second sentence VPRA are not sure what the author is saying here, because diagnosis of the condition is not wholly dependent on serious bleeding, though this is often the most obvious and visible indicator. However as the condition can present asymptomatically – (hence, the reason why ultrasound is the most reliable method of making the diagnosis - with or without bleeding) – VPRA are unclear why an examination of the placenta and umbilical vessels would prevent a post natal diagnosis in the hitherto asymptomatic pregnancy. The final sentence is agreed, indeed as compression on the velamentous vessels or vasa praevia occurs - this can restrict growth, SGA etc. and this might be considered as another warning sign?
	2(iii) Recognised latent period or early symptomatic stage	
	The "latency" of vasa praevia relates to the antenatal period from the time that the vasa praevia develops in utero. This is the basis of ultrasound screening for the condition.	
	There is no accepted early symptomatic stage, but bleeding in pregnancy could be considered a possible alert system for vasa	NB. this is not entirely correct – as the author acknowledges in footnote 17 – however it is VPRA's position that the diagnosis is best made in the

	previa. This is likely to have a low positive predictive value given the relative common occurrence of vaginal bleeding in pregnancy.	second and/or third trimester. VPRA are also unsure about the validity of the assertion that bleeding would have a low predictive value. Perhaps the key here is to have a greater awareness of suspect vasa praevia cases, and to note that, in the main, in vasa praevia cases the bleeding is painless and armed with a higher clinical suspicion of vasa praevia generally – bleeding may present yet another opportunity to make the diagnosis, by use of testing for fetal haemoglobin (HbF) by the use of very simple blood analyses i.e. Apt, Ogita and the easy to use method described by Pelle G. Lindqvist & Peter Gren – *European Journal of Obstetrics & Gynecology and Reproductive Biology 131 (2007) 151 – 153*. See also Odunsi et al - *Evaluation of Chemical Tests for Fetal Bleeding from Vasa Previa – Int. J. Gynaecol Ostet. 1996 Dec;55(3):207-12*. Notwithstanding the relative common occurrence of vaginal bleeding in pregnancy, where it is known that the pregnancy is one which falls within the accepted risk groups (stated herein) if such a blood test were given to a pregnant woman who presented with bleeding, this would increase the positive predictive value given the sensitivity of the tests to fetal haemoglobin. NB. It should always be stressed to the public that though common such bleeding IS NOT NORMAL as midwives and doctors are too prone to say.
	3 Any cost-effective primary prevention interventions practicable?	
	Primary prevention of the actual condition is not feasible given the developmental nature of vasa previa, but a reduction in fetal mortality and morbidity is possible by the avoidance of the resultant fetal haemorrhage through prenatal recognition and alternative delivery by the abdominal route (caesarean section). There is no reported increased risk of recurrence of vasa praevia in a subsequent pregnancy.	NB. Though this is of course correct, it does rather understate the position – which is that there would be a reduction of mortality from 56% to at least 3% in cases diagnosed antenatally. VPRA can think of few clearer statements of benefit outweighing harm. (see paragraph 13 below). It should be noted that in the event of an infant surviving undiagnosed vasa praevia – the prognosis is often very bleak with inter alia poor Apgars, cerebral palsy, heart and/or renal failure very common.

	The Test	
	4 Simple safe precise and validated screening test	
	The first ultrasound description of vasa praevia dates back to 1987[12]. Assessment of the placenta using ultrasound is already included within departmental ultrasound protocols as advised by the RCOG. Ultrasound examination for insertion of the placental cord has been advocated as a screening test in all pregnancies. Ultrasound diagnosis is considerably simplified by employing a colour Doppler facility over the cervix[13], with transvaginal images being superior to an abdominal scan (given the closer proximity to any vessels over the os and easier recognition of vessels in the coronal plane). Cases with a three-dimensional ultrasound diagnosis of vasa praevia were published in the literature in 2004[14]. 3D ultrasound is not universally available and is not considered necessary for prenatal screening using ultrasound. Although 3D scanning can help in the accurate localisation of aberrant vessels around the internal cervical os and can be useful in the therapeutic approach[15], arterial and venous blood flow can still be recognised at the time of the 2D fetal anomaly scan.	NB. whilst this would indeed represent a gold standard, it is far simpler to consider putting a flash of colour Doppler over the internal os in all routine obstetric scans. This would identify almost all placenta praevia cases and/or those cases with suspicious vessels. Thereafter the diagnosis or exclusion of vasa praevia can be confirmed by later review especially where suspect vessels have been identified by this screening process. This is the view expressed in the current UKAS obstetric guidelines [now part of the College of Radiographers]. Transvaginal scans, though more sensitive, are not necessary for the identification of vasa praevia. However in obese patients or when the fetus is in an awkward position TVS is, with the patient's consent, the better option. Additionally TVS is by far the better option in terms of image resolution, and is likely to be the preferred option in follow up scans in cases where vasa praevia is either suspected or for some reason cannot be excluded. Given that most UK sonographers performing the anomaly scan are proficient in 2D scanning and that vasa praevia can be accurately diagnosed without recourse to 3D - there is no need for the use of 3D.
	Ultrasound testing for vasa praevia has not been validated using randomised studies. However the presence of a velamentous insertion or a bilobed placenta should lead to the exclusion of a vasa praevia. This would appear to be the first stage in the diagnostic pathway.	With regard to the first sentence, if it is the NSC's position that a randomised control study would be useful - what proposal does it make to carry one out? This is important as when questioned recently on this subject the Prime Minister responded unequivocally that the Government have; *"...a very very big programme of health service research, it's*

		about £1.7 billion over the next 10 years. Research into [vasa praevia] is part of it..." [YouTube: Ask the PM – Vasa Praevia]. If this is correct who, when and what form will a prospective or other such study take? Given that the current anomaly scan is silent on screening for vasa praevia, which in turn leads to the condition being an emergent one, how does the NSC envisage such a prospective study might be designed? What evidence does the NSC consider it would derive from any such study that it does not already know or have access to? A problem envisaged by VPRA is that the exclusion of a certain group in any proposed randomised control study would or may be ethically unsound – hence given the great preponderance of sound retrospective studies, case reviews and reports ALL of which report an almost 100% success rate upon antenatal diagnosis as opposed to the dismal outcome in the absence of antenatal diagnosis – it cannot be that the lack of an unspecified prospective study – which in all likelihood would not be possible - should present as a bar to commonsense. With regard to the second sentence we agree but it should also be stated that the presence of a placenta praevia should likewise lead to an exclusion of vasa praevia – this is of paramount importance – see for example; Oyelese, Ultrasound Ostet. Gynecol. 2001; 18: 96-99; and Fung & Lau, Ultrasound, Obstet. Gynecol 1998; 12:430-3 With regard to the final sentence whilst we agree that there should be clear pathways to diagnosis, would not the first (and most cost effective) stage of screening be to include in all anomaly scans a simple flash of colour Doppler over the internal os? If this were carried out in all anomaly scans it would, in all probability, reveal all cases where there was a placenta praevia which could be referred in the normal way. However in all other cases it would reveal the presence or otherwise of suspicious fetal vessels, which if found could be properly reviewed and thus lead to a diagnosis or exclusion of vasa praevia. Likewise a finding of velamentous insertion, would or could, in the same

		way, lead to a further review of the patient.
	(a) Screening for Velamentous Insertion in the First Trimester	NB. The NSC and the author should consult with Mr. Christopher Griffin, Consultant Obstetrician – Heart of England NHS Foundation Trust - as we understand that he has data on a large number of first trimester scans wherein he routinely screens for velamentous insertion. Additionally he has often confirmed the diagnosis of vasa praevia or velamentous insertion by later pathology. However whilst the following material is of some interest, VPRA's position is that though it is indeed possible to make the diagnosis of vasa praevia in the first trimester, it is better to attempt the diagnosis in the second and/or third trimester. The simple rationale being that more pregnant women take up the option of screening at this time and as it adds little in terms of cost or time to the current anomaly scan this is the optimum time for screening.
	The option of exploring the cord insertion during the first trimester nuchal translucency scan[16] has been explored. Out of 533 consecutive pregnancies screened the prevalence rate of velamentous insertion was 0.9% with the diagnosis confirmed at the time of the second trimester scan and also at delivery. It has been suggested that the fetus is less likely to obscure the cord insertion at that time. In a prospective study, Hasegawa et al[17] looked at the cord insertion site between 9-11 weeks of pregnancy in 340 cases and were able to demonstrate the cord insertion in 93.5% of cases. The cord insertion was seen to be in the lower third of the uterus in 11% of cases (n=35), and in these there was an association with frequent developmental abnormalities of the placenta and cord, 29% of the cases with a low cord insertion having a velamentous or marginal cord insertion at delivery (compared to 1.4% where the cord insertion was seen not to be low in the first trimester). The relative risk of vasa praevia with a low cord insertion at 9-11 weeks was 9.32. There were no low-lying placentas in the group (283 cases) where the cord was seen to be inserted normally. The authors	NB. For precisely the reason that most of the women in the UK who have an obstetric scan have a 2nd trimester scan, this is why the diagnosis is best made routinely at that stage. However this should not discourage those performing 1st trimester scans from seeking to visualise aberrant fetal vessels or vasa praevia where possible.

	considered that this was a useful tool to identify high risk pregnancies. However Derbala et al[18] conclude that a vessel seen during a first trimester transvaginal scan should not be assumed to be a vasa praevia, as often the vessel is of maternal origin. Although a comparison with the maternal pulse should aid differentiation the authors advise that the diagnosis of vasa praevia is best made in the 2nd and 3rd trimesters, and that if a suspicious vessel is found in the first trimester a repeat scan in the second trimester is suggested. At present there does not seem to be any additional advantage in seeking to establish the cord insertion in the first trimester of pregnancy, especially given that currently more women have a detailed second trimester rather than a detailed first trimester ultrasonic assessment. Second trimester screening for velamentous insertion has been explored in greater detail. A diagnosis in the second trimester will still allow for preventative measures to be taken in time to improve the prognosis for the fetus.	
	(b) Screening for Velamentous Insertion in the Second Trimester	NB. The author's analysis of the literature reveals that the screening methodology is simple, cheap, quick, precise and reproducible. Insofar as the work is applicable to screening for vasa praevia, we comment on the general "commentaries" below;
	Prospective work indicates that placental cord insertion and velamentous insertion (pre-requisites for the prenatal diagnosis of vasa praevia) can consistently be identified with colour Doppler imaging during routine mid trimester fetal anomaly scans. Sauerbrai et al[19] reported two cases of an antepartum diagnosis in 1998 using endovaginal colour Doppler and power Doppler ultrasound.	We agree
	Nomiyama et al (1998)[20] concluded that 99.8% of all cord insertions were identifiable prospectively using colour Doppler during the routine mid trimester	Nomiyama et al (1998) is evidence firmly in favour of the reliability of screening for velamentous cord insertion. Furthermore the mean time to visualise the cord insertion was 20 seconds, and in 95% of

	fetal anomaly scan. They looked at 587 cases in an attempt to identify the umbilical cord insertion, velamentous cord insertion and vasa praevia. The specificity of velamentous cord insertion identification was 99.8% (580/581 cases) with a sensitivity of 100% (5/5 cases). The positive predictive value of velamentous cord insertion was 83% (5/6 cases) and the negative predictive value was 100%. There is a question as to whether to include marginal placental insertion as an assessment of cord insertion as the significance of this condition is more questionable. The reliability of the sensitivity of the screening test is also questionable given the difficulty in obtaining accurate outcome data as referred to earlier. An older prospective study[21] indicated that ultrasound identification of a velamentous or marginal cord insertion had a sensitivity of 42%, specificity of 95%, a positive predictive value of 67% and a negative predictive value of 12%. However grey scale sonography appears to have been employed in the main with selective recourse to colour Doppler which was described as being helpful to identify the exact location of the cord insertion. On this basis, the rate of visualisation of the cord insertion was 54% in a busy routine clinical practice which increased to 67% in a retrospective analysis of cases scanned between 15-20 weeks of pregnancy.	cases cord insertion was visualised in under 1 minute. With regard to the fifth sentence VPRA are unsure why this is stated because in the Nomiyama study the sonographic and pathological findings differed in only two cases (page 428). With regard to the reliability of the Pretorius et al study which is now over 10 years old it should not be overlooked that the available technology used in the study would now be vastly improved. However notwithstanding the technological restrictions in the study it is worthy of note that the sonographic assessment of the cord insertion in this study correlated to pathologic outcome in 83% (106/128) of singleton pregnancies. Author's conclusion: [We] could consistently identify cord insertion and velamentous cord insertion with colour Doppler imaging during routine sonography in the mid trimester and transvaginal colour Doppler imaging and serial scans were needed to identify vasa praevia.
	Sepulveda et al[6] looked at 832 pregnancies and also sought to establish on a prospective basis the feasibility of identifying velamentous insertion of the umbilical cord during routine obstetric ultrasound. Using colour Doppler they were able to confirm the cord insertion in 99% of cases with 8 cases of velamentous insertion (1%). Out of these 8 cases velamentous insertion was later confirmed in 7 at delivery (the eighth being a marginal insertion). The authors concluded that systematic assessment of the placental cord insertion site at routine obstetric ultrasound has the potential to identify	Sepulveda's prospective study conclusively confirmed the reliability of routine screening for velamentous insertion of the cord. It also confirmed that in 95% of the cases visualisation of the insertion of the cord took less than 1 minute with a zero false negative incidence. Author's conclusions: Velamentous insertion of the umbilical cord can reliably be detected antenatally by grey scale and colour Doppler. Systematic assessment of the placental cord insertion site at routine obstetric ultrasound has the potential to identify pregnancies with velamentous insertion, and therefore those at risk for vasa praevia.

	pregnancies with velamentous insertion, and therefore those at risk for vasa previa.	
	The largest published study (Lee et al, 2000)[2] consists of 93,874 cases. This looked at prenatal ultrasound diagnosis and clinical outcomes of vasa praevia over an 8 year period but on a retrospective basis and using a variety of ultrasound systems. Colour Doppler was used to evaluate suspicious appearances. 18 cases (0.02%; 2:10,000) of vasa praevia were initially suspected and serial scans used to characterise the natural history of vasa praevia. Three (16.7%) had normal late trimester scans and were delivered vaginally (initial false positives in the screening pathway). The rest were delivered by planned and uncomplicated caesarean section. The main pathology findings were velamentous cord insertions. Neither the sensitivity not the specificity of ultrasound for diagnosing vasa praevia could be assessed. The authors advocated the identification of asymptomatic patients followed by delivery at 35-36 weeks and after an amniocentesis to check on fetal lung maturity.	This study was retrospective and collected data from 1991 – 1998 by grey scale ultrasound – no uniformity of equipment used, and as above the technology has improved significantly since this date. Eight cases initially showed the placental edge over the internal os and later developed vasa praevia after the placenta receded from the cervix. With regard to the fifth sentence, whilst VPRA are unsure of the percentage quoted, and not doubting it, this readily demonstrates that there should little or no increased risk of caesarean section in the event of an initial false positive. Author's conclusions: Vasa Praevia was detected in asymptomatic women as early as the second trimester. Perinatal outcome was generally favourable, although some infants had slightly extended newborn nursery admissions due to mild complications of prematurity.
	Catanzarite et al[4] looked at the specificity of ultrasound diagnosis of vasa praevia. This study involved the prospective collection of vasa previa cases diagnosed using colour Doppler. 11 cases were identified out of 33208 over an eight year period (0.03%; 3:10,000). They confirmed 10 cases at delivery (91% sensitivity; one false positive diagnosis) of which 2 were related to velamentous cord insertion over the cervix and 8 linked to low-lying placentas. The authors could not assess the specificity of ultrasound diagnosis of vasa praevia as they did not have outcome data for all the pregnancies scanned. The number of perinatal deaths avoided would be estimated according to the perinatal mortality ascribed to vasa praevia. The authors advocated delivery after demonstration of fetal pulmonary maturity and prior to the onset of labour.	VPRA are not sure that there was ever a false positive or whether the eleventh case was simply not confirmed by the delivering obstetrician. NB. Medline confirms the specificity of diagnosis as 91%. Author's conclusions: Antenatal diagnosis permitted [us] to prevent catastrophic outcomes commonly associated with vasa praevia.

	Hasegawa et al[21] looked prospectively at umbilical cord insertion in 3446 cases at 18-20 weeks gestation and concluded that pregnancies with velamentous cord insertions were associated with intrapartum complications including fetal heart rate abnormalities and low Apgar scores. They suspected a velamentous insertion in 40 subjects (1.2%) and marginal cord insertion in 39 cases (1.1%) amounting to 79/3446 cases (2.29%). Antenatal detection of velamentous cord insertion had a sensitivity of 62.5%, a positive predictive value of 100% and a negative predictive value of 99.6%. In a later publication in 2007[10] the same authors highlighted how umbilical cord insertion to the lower uterine segment is a high risk factor for vasa praevia.	NB. Footnote numbering is incorrect? The later study in 2007 quoted as footnote 10 provides support for those engaged in first trimester scans, see above and for which further support and assistance for sonographers can be found for those using the Astraia software database. In 2009 it is hoped that Viewpoint will also introduce similar fields for the recording of umbilical cord insertion 10w – 13w+6d and subsequent scans.
	In Nomiyama's series[20], 2 cases of vasa praevia were identified prenatally between 18-20 weeks in a total of 587 cases (with 5 cases identified as having a velamentous cord insertion) and 1 was confirmed at delivery. In the other the vasa praevia could not be identified at the time of the repeat scans at 30 and 36 weeks and a normal vaginal delivery ensued. Aberrant vessels might regress from the cervix in some women in late pregnancy on the same way as placental tissue can migrate from the lower uterine segment as the pregnancy progresses as a result of differential growth. In this series the "false positive" rate at 18 weeks was 50% limiting the midtrimester Doppler studies to the abdominal route. By comparison, the "false positive" rate in the Lee paper was 16.7%, although this is a false positive in the context of findings in the second trimester compared to the third, with exclusion occurring before obstetric intervention (i.e. not true false positives in terms of the final diagnosis.	This is not agreed – it is highly unlikely that aberrant vessels will "migrate" in the same way as placental tissue might. There is simply no evidence for this statement – if the vessels are not there on a follow up scan it is far more likely that the earlier diagnosis of a vasa praevia was incorrect. In the Nomiyama study the "false positive" diagnosis at 18 weeks was not confirmed at 30 and 36 weeks allowing for a normal vaginal delivery. For comments on the "false positive" rate in the Lee et al paper see above, but we note none of the false positives quoted have lead to obstetric surgical intervention.
	Case reports describing prenatal diagnosis of vasa praevia using colour Doppler ultrasound were published in 1998[22]. A transabdominal sweep with the pulsed colour Doppler will usually detect abnormal	?? Footnote numbering?? This is the view taken by VPRA – however due to the erroneous numbering, we are unable to ascertain which case report is referred to herein.

	vessels over the cervix, and any identifiable colour flow (indicative of vasa praevia) would then warrant additional investigation.	
	Proponents of screening advocate a short sweep with colour Doppler over the internal cervical os only in cases where the initial 2D fetal anomaly scan shows that the placental cord insertion and the lower margin of the placenta are not clearly away from the internal cervical os. The test would be carried out as part of the midtrimester fetal anomaly scan but can be carried out later if the woman presents for antenatal care at a later gestational age.	This is clearly a reference to the algorithm developed and advocated by Philippe Jeanty MD. PhD [see: Derbala Y Grichal F Jeanty P, J Prenatal Med 2007; 1(1):2-13; and http://www.thefetus.net/listing.php?id=2183]. It is also the view of VPRA that the simplest method to screen the general population in the context of the 20 week anomaly scan is to place a short sweep of colour Doppler over the internal cervical os in all cases. This should identify both placenta praevia and vasa praevia cases. In either case a referral as a high risk pregnancy would be necessary. And given the above findings of Lee et al and also Nomyima et al (supra) there must be a high degree of confidence that any early false positive diagnosis [of either condition] can be confidently excluded prior to any unnecessary obstetric operative intervention.
	Colour flow Doppler screening is also advocated in circumstances where there is an increased risk of vasa praevia (succenturiate lobe, multilobate placenta, velamentous insertion, multiple pregnancy, low-lying placenta or an IVF pregnancy). In a study of a large number of affected cases[5] 32.2% of women had bilobed or succenturiate lobed placentas and 61% had second trimester low-lying placentas. In 20% of these the placenta remained low-lying at the time of delivery. The proportion of women having third trimester vaginal bleeding was 36.1%.	NB. Given the purported lack of "prospective" studies VPRA's suggestion is that there is ample retrospective and case review evidence to commence screening for those in known risk groups. It is VPRA's view that this would provide a useful starting point for the collection of data. There are clearly groups at an increased risk (identified above) not least IVF pregnancies which on any view at 1:300 is an unacceptably high incidence [see generally; Burton & Saunders; *Aust NZ J. Obstet Gynaecol; 1988; 28(3):180-1;* Oyelese et al; *J Matern Fetal med 2000 Nov-Dec; 9(6):370-2;* Schachter et al; *Fertil Steril. 2003 May; 79(5):1254-5;* Bhide & Thilganathan *Current Opinion in Obstetrics & Gynecology 16(6):447-451 – December 2004*]. It is also evident that most vasa praevia cases are associated with placenta praevia in the second trimester (odds ratio = 22.86; Baulies et al supra) – and given that all women identified as having a placenta praevia at 20 weeks should be managed

		as high risk pregnancies in accordance with RCOG Greentop Guideline No 27 – it is VPRA's suggestion that the NSC should recommend that this Guideline should be extended to provide for screening of those women who fall into the known risk groups for vasa praevia likewise between 32 and 36 weeks.
	Abdominal wall scarring, a high maternal body mass index or an incompletely filled maternal bladder may limit the screening process. Detection of fetal vessels within the membranes may be limited by maternal size, the status of the maternal bladder and the direction of the velamentous vessels. False positive results can arise from motion artefacts (e.g. amniotic fluid movement resulting from fetal movement). Under these circumstances any flow is irregular in nature and lacks reproducibility. This is known as "flash artefact" which can be recognised by repeating the examination once the movement had subsided. A false positive result can arise from an umbilical cord presentation which would mimic the Doppler appearances of vasa praevia. In order to distinguish a cord presentation it would be necessary to attempt to shift the position of the umbilical cord by gently tapping with the ultrasound transducer over the area in question. The use of colour Doppler can differentiate from similar ultrasound appearances due to other causes such as marginal placental sinus, a normal umbilical loop, chorioamniotic membrane separation (which can occur normally up to 16 weeks), cervical varicose veins and simple folds of the membranes. Whereas a marginal placental sinus may present with flow, this can be differentiated by comparing the rate to the maternal heart frequency.	Motion artefact is often quoted as a pitfall in diagnosis but it is easily identified. Anyone confusing a flash or motion artefact for a suspect fetal vessel can exclude this by simply noting the irregular duration and interval of the flash or motion artefact. Should doubt persist dropping a pulse wave Doppler sample over the suspicious vessel will confirm whether it is a fetal vessel. Funic presentation is unlikely to be confused as a vasa praevia but it is also excluded simply by tapping over the area of the cord to see if it moves. NB. All of these "pitfalls" or routes to misdiagnosis are easily avoided by reference to the presentation VASA PRAEVIA by Dr. Philippe Jeanty MD. PhD and available free of charge via www.the Fetus.net – see lectures; http://www.thefetus.net/listing.php?id=2183.
	If the colour Doppler test is not normal a transvaginal scan is then advised. Transvaginal scans do not cause or worsen vaginal bleeding in suspected cases. In addition transvaginal ultrasound may be required in obese women, those with scars	This again is not referenced but is plainly a reference to the algorithm developed and advocated by Dr. Philippe Jeanty MD. PhD [see: Derbala Y Grichal F Jeanty P, J Prenatal Med 2007; 1(1):2-13; and http://www.thefetus.net/listing.php?id=2183], and

	or if the fetal presentation is difficult. If normal then the pregnancy is categorised as low risk for vasa praevia.	also advocated by VPRA.
	If the transvaginal colour Doppler test is abnormal or suspicious then it has been suggested that the pregnancy be managed as for vasa praevia.	See comment above.
	The effectiveness of ultrasound screening for vasa praevia is unproven, with conflicting evidence over its reliability. Eddleman et al[23] retrospectively looked at 82 cases of velamentous cord insertion out of study population of 16210 cases and concluded that routine non-targeted obstetric ultrasound failed to detect any cases of velamentous cord insertion, including three cases of vasa praevia. They concluded that the potential for pre-emptive obstetric intervention appeared to be limited and went on to conclude that failure to diagnose apparent velamentous cord insertion during a routine ultrasound did not appear to be a departure from the standard of care. However crucially the ultrasound scans performed on the patients later shown to have a velamentous cord insertion did not specifically assess the umbilical cord insertion site. Later, and on a retrospective basis, Heinonen et al[24] were only able to directly visualise the abnormal insertion successfully in 1 of 73 cases of velamentous cord insertion using conventional obstetric ultrasound without colour Doppler application. There were no cases of vasa praevia during that particular study period.	VPRA do not accept that the effectiveness of ultrasound screening is unproven. Whilst there have been no prospective studies specifically to look at screening for vasa praevia – the predonderance of all of the literature is overwhelmingly in support of routine screening. The Eddleman et al study is of limited or no value in the context of this review when one bears in mind the work of Nomyima et al, Lee et al and Hagesawa et al *supra*. These studies are of limited or no value in the context of this review when one bears in mind the work of Nomyima et al, Lee et al and Hagesawa et al *supra* indeed it is worthy of note that this study is 17 years old and has by today's standards obvious limitations in respect of the available technology [cf. later studies]
	Some cases are likely to be missed. Visualisation of the vasa praevia may be difficult with transvaginal ultrasound alone as the vessels may run at an unfavourable angle to the transducer, and a more favourable angle might be achieved using the transabdominal route. Whereas the initial false positive rate can be as high as 10-16%, this can be reduced by repeating the ultrasound examination in the third trimester.	The most common misunderstanding made by most observers about the proposed introduction of routine screening for vasa praevia is that it will have an immediate effect and be a faultless process. This is misconceived, as with any diagnostic screening process there will be cases that will be missed, even where care is taken – there will be false positives – but as has been seen in the prospective and retrospective studies above, these are likely to be resolved long before any obstetric intervention. There will also be false negatives – though one envisages that this will

		occur far less than at the current rate which is almost at 100%. Awareness and training are key factors in ensuring the screening process is as effective as possible. VPRA do not advocate routine TVS (see above), TAS would in most cases be sufficient to make the diagnosis. In all the studies referred to herein the "false positive" diagnosis rates are neutralised by routine obstetric review usually in the third trimester, which makes screening for vasa praevia ideal for inclusion in the anomaly scan as there is already a built in review at 32 weeks for all those with placenta praevia. It would require little by way of resources to include vasa praevia cases at that stage.
	(b) Screening for Velamentous Insertion in the Third Trimester	
	Others[25] have suggested that the diagnosis of vasa praevia could be incorporated into third trimester scans to explore the low lying placenta identified at 20 weeks of pregnancy especially where the placental edge covers the os in mid pregnancy but recedes later on. This would seem to be the basis for selective but not routine third trimester screening. In Sepulveda's study[6] any failures of imaging for velamentous cord insertion occurred in the third trimester.	Footnote numbering??? This is correct but as vasa praevia is very closely associated with second trimester placenta praevia (see Baulies et al) this would seem to be a logical extension of RCOG Greentop Guideline No.27, namely to require the exclusion vasa praevia even in cases where the placental edge has receded on a third trimester review of an earlier diagnosed placenta praevia case. NB. by suggesting some form of selective screening for those in risk groups this should not be taken as any indication that screening for vasa praevia should not be routine in all 20 week obstetric scans. VPRA are not sure about the assertion that there were failures to detect velamentous insertion in the third trimester, but we are certain that in this study where velamentous insertion was found it was always found prior to 30 weeks.
	There is one published case report[26] which indicates that in a less skilled environment the diagnosis can be missed even in the	VPRA assumes this is a reference to Lijoi & Brady (see incorrect footnote numbering). This case report readily demonstrates that where, as in this

	presence of risk factors. The authors point out that the accuracy of transvaginal flow Doppler in diagnosing vasa praevia is unknown, with antepartum diagnosis not eliminating morbidity and mortality. The authors concluded that there needs to remain a high index of suspicion for vasa praevia at the time of amniotomy because not all cases can be diagnosed before the onset of labour.	case, there were no protocols to follow the sonographer was not therefore looking for evidence of vasa praevia – hence it was not seen. Perhaps this is a statement of the obvious – and with respect to Drs. Lijoi & Brady, though the links between bi-lobed or succenturiate lobed placenta and vasa praevia had been well documented in the literature prior to their case report – if they were not considered or a protocol followed antenatal diagnosis was unlikely to follow. In so far as the "accuracy" [unsure what this means] of transvaginal flow Doppler in the diagnosis of vasa praevia is concerned – this cannot really be in dispute
	More recent publications have not provided additional evidence for screening but have served as a vehicle for promoting widespread incorporation of universal screening for vasa praevia[x].	"X" This is not referenced, however it is also not entirely accurate because the most recent published study S. Baulies et al; Prenat Diagn 2007; 27:595-99 Prenatal ultrasound diagnosis of vasa praevia and analysis of risk fators – has provided more support and evidence towards routine screening. It concluded that second trimester screening enabled the authors to avoid any prenatal or neonatal death following prenatal diagnosis of vasa praevia in a five year period. The study also identified risk groups for the condition by multivariate analysis. It also calculated odds ratios for the idenfied risk gropus; IVF (7.75); Bilobed or succenturiate placenta (22.11); and second trimester placenta praevia (22.86).
	In a recent comprehensive review of vasa praevia Derbala et al[18] suggest that whereas in their opinion it is unlikely that all cases of vasa praevia will be recognised, awareness of the risk factors and adoption of a protocol to specifically seek vasa praevia plus careful examination should substantially decrease the number of unsuspected cases at delivery, and that barring technical problems of maternal obesity or scarring, a majority of cases – quoted as 90-95% - should be recognised.	A view shared by VPRA. Additionally the authors of this review concluded a prognosis of; 1. a perinatal mortality rate of 56% in undiagnosed cases as opposed to 3% in diagnosed cases. 2. Median Apgar scores of 8 & 9 (at 1 & 5 minutes) when diagnosed as opposed to 1 & 4 for undiagnosed (survivors). 3. Transfusion required in 58% of newborns not diagnosed as opposed to 3% when diagnosed antenatally. (see also Oylese et al, *supra*) The obvious conclusion reached was; ***"..until proven otherwise, .. substantial improvement in outcome will depend ONLY on prenatal detection.***

		<u>This implies a greater awareness of the condition and an effort at detecting it..”</u>
	5 Distribution of test values in target pop and suitable cut-off	
	There are no numerical test values since the screening examination using ultrasound would be a subjective exercise (the actual examination). Under these circumstances there would not be a formal numerical cut-off.	
	In cases where the ultrasound scan identifies that the cord insertion is central, there is no succenturiate lobe and the placenta is away from the cervical os, then the likelihood of vasa previa is considered to be negligible and no further assessment for vasa praevia is necessary. The pregnancy would then be classified as being at low risk of vasa praevia.	This is the view of VPRA
	Fung & Lau[8] suggest that given the high association between vasa praevia and low-lying and bi-lobed placentas (with low-lying placentas in 81% of cases of vasa praevia) specific targeted ultrasonography should be considered. Other high risk groups include multiple pregnancy and in vitro fertilisation along with those women who have had previous uterine surgery. This approach has been supported by others[23]. The introduction of guidelines relating to screening of all IVF-embryo transfer pregnancies with transvaginal ultrasound and colour Doppler in the second trimester to rule out vasa praevia has been advocated[28].	Given the acceptance herein of the recognised risk factors VPRA believe that a failure to introduce screening for women in these recognised risk groups is unacceptable and the chance to introduce this screening as minimum standard must not be missed. All of these conditions are suitable for selective screening of higher risk routine screening – but informed consent for those patients must also be provided – so such parents can elect for screening themselves. This is also a logical extension of RCOG Greentop Guideline No. 27
	6 Test acceptable to population	
	In 2006-07 451,987 mid pregnancy fetal anomaly scans were recorded in England with data coming from just over half the hospitals in the country that provide antenatal screening services. These hospitals reported an average uptake of fetal anomaly scans of 97.2%.	
	The overwhelming majority of pregnant women therefore accept the offer of a	Nearly 100% of women accept the mid trimester scan. The purpose of which is to identify fetal

	midtrimester ultrasound scan for fetal anomaly, and with appropriate counselling do so in the expectation that they will obtain reassurance and that any abnormalities can be identified in the antenatal period. In this respect an initial screening test for vasa praevia would be expected to fit under the umbrella of the routine fetal anomaly ultrasound scan.	anomalies, with that in mind it is important to note; 1. Vasa Praevia is not an anomaly in the sense that diagnosis of it would lead to counselling towards termination of the pregnancy, as would be the case in event of the discovery of other fetal anomalies routinely screened for. 2. Nor is the antenatal diagnosis generally otiose in the sense that other anomalies with a similar prevalence i.e. facial cleft (1:1000) – which are quite properly screened for, but are not life threatening and for which nothing can be done to prevent delivery of the fetus with the condition. 3. Put another way diagnosis of vasa praevia is the key to the baby's survival – and VPRA cannot conceive of a situation where a prospective parent would not wish to have this information.
	There are no studies which identify whether a screening test for vasa praevia would be acceptable to the general population, and it would also be reasonable to assume that a majority of the general population is unaware of the condition of vasa praevia. General education of the public would therefore be highly desirable in order to meet requirements for informed consent. However the process of agreeing to a fetal anomaly scan does not require mothers to have a detailed knowledge of all the potential abnormalities that can be identified, rather than they have an understanding of the rationale behind the midtrimester ultrasound scan itself.	In relation to the third sentence herein VPRA are not sure what the author is stating, however, if it is, as it appears to be, that parents do need not know about vasa praevia – then it is a mistake, a potentially very costly mistake. Of course no one would expect a parent to have a detailed knowledge of all of the potential abnormalities – but one does expect a sonographer to have this knowledge. Take this as an example; upon discovery of a low lying placenta what is the sonographer's <u>current</u> remit? It is of course to refer the patient for a further scan at 32 weeks. What if the placenta has receded at 32 weeks? It is to give advice that it is safe to have a vaginal delivery (and often this is the correct advice), however sadly time and time again VPRA are contacted by parents who were given and took this advice – only to discover – too late – that the sonographer – limited their informed consent – by not advising them of vasa praevia and the associated risk with low lying placenta – VPRA believe that a continuation of this policy would be actionable as clinical negligence. It makes little sense to scan women with low lying

		placentas at this stage and not check for aberrant vessels over the internal os.
	A vaginal scan is not normally carried out at the time of the midtrimester fetal anomaly scan which is performed using the abdominal route. Transvaginal scanning is more invasive and will also require additional time. Proponents of screening suggest that a transvaginal approach be limited to specific cases where there already is a high index of suspicion (e.g. IVF, multiple pregnancies, abnormal flow).	See comments above TVS is NOT required for screening, save in exceptional cases or with consent on review of the case at a later stage (cf. The current RCOG Greentop Guideline No.27)
	Early diagnosis can lead to additional parental anxiety, as can a prenatal diagnosis of velamentous insertion without vasa praevia. Parental education will potentially introduce a degree of anxiety in an area where a majority of the general public remain on the whole ignorant of vasa praevia. The impact on maternal anxiety and any accompanying responses (e.g. pressure on clinicians to effect a preterm delivery by caesarean section) has not been assessed but is an important area that needs to be evaluated.	VPRA believe that all prospective parents are anxious irrespective of how many children they have or have had. If nearly all women accept midtrimester screening, all or most must by definition accept the risk of being given news that may require counselling or reassurance. Ignorance of the existence of a condition such as vasa praevia, which if diagnosed would mean the survival of the unborn child, is simply not comparable to the following; 1. A continued ignorance of the same condition which left undiagnosed in turn leads to the death of a child at or near term, and thus the serious psychological harm that this will cause to the mother and her family; 2. Knowledge of the condition which with informed consent will lead to the proper management of the pregnancy in a controlled way, albeit with an increase in anxiety; 3. Any perceived or real increase in pressure on a clinician to exercise clinical judgment.
	7 Agreed policy on further diagnostic investigation/choices	
	Prenatal diagnosis allows for the closer monitoring of symptoms of vaginal bleeding and facilitates planned delivery under controlled circumstances. Proponents of screening recommend serial scans,	The first sentence is agreed. The second sentence is not agreed, if it is intended to apply to VPRA. We have set out clearly both here and on our web site that routine screening in

	decreased or limited maternal activity, "pelvic rest" and close attention to early signs of labour or bleeding when vasa praevia is suspected. Some advocate hospitalisation from 32-34 weeks (although the cost effectiveness of this approach was not evaluated), with corticosteroids to aid lung maturity when the cervix is not long and closed. However hospitalisation is not an approach that is advocated in the UK when faced with other similar clinical problems, and nor indeed is the use of amniocentesis specifically to assess fetal lung maturity[29]. Others[5] have suggested the use of serial transvaginal cervical length determinations along with hospitalisation should the patient experience uterine contractions or vaginal spotting. Nogiyama et al[20] advised repeat ultrasound scans at 30 and 36 weeks and it was at this stage that transvaginal Doppler was employed if the cord insertion site could not be visualised by the transabdominal route.	the second trimester should act as a filter to weed out all suspected cases of vasa praevia. After that VPRA would advocate further scans as often as clinically advised, however we would argue for at least one follow up scan at or about 32 weeks, to confirm the diagnosis. [Similar to the suggestions made by most commentators cf. Nomiyama et al]. However anecdotally we are aware that most clinicians will require more than this. We would advocate hospitalisation – but the role of this review is not to assess management but to assess screening or other diagnostic investigation. Nonetheless it is evident from the literature that vasa praevia cases habitually rupture at or prior to term, and to avoid the concomitant risk of fetal demise or compromise – hospitalisation in the third trimester is recommended. The fourth sentence is specifically NOT accepted. RCOG Greetop Guideline No. 27 states; *Antenatal management* *Women with major placenta praevia who have previously bled should be admitted and managed as inpatients from 34 weeks of gestation. Those with major placenta praevia who remain asymptomatic, having never bled, require careful counselling before contemplating outpatient care. Any home-based care requires close proximity with* *the hospital, the constant presence of a companion and full informed consent from the woman.* VPRA does not believe that a true vasa praevia is any less life threatening for the unborn infant than a major placenta praevia and thus hospitalisation is an approach that is advocated in the UK when faced with other similar clinical problems. VPRA believe vasa praevia could and should be treated in the same way.
	8 Effective treatment or intervention	
	The overall perinatal mortality in a recent series of 155 cases of vasa praevia (the largest reported) was 36% (55/155)[5]. This series was however limited by selection bias with a number of cases registering through the Vasa Previa Foundation. Within this series 39% (61/155) of cases were diagnosed prenatally, thereby avoiding fetal vessel rupture at or near delivery. The	In respect of the seventh sentence VPRA are unsure of this hypothesis – which we understand to be stating as follows; The studies refer in the main to un-ruptured vasa praevia (due to antenatal diagnosis by ultrasound) – what is not known is how many diagnosed cases (by ultrasound) would have, if managed, resulted in rupture during labour.

	perinatal mortality when the diagnosis was not made prenatally was quoted at 56% (i.e. 44% survival) compared to 3% (i.e. 97% survival) in those diagnosed prenatally. This is in keeping with older estimates of perinatal mortality in cases of undiagnosed vasa praevia of 50-70%[30], with others quoting figures varying between 22.5-73%. The combination of mortality and morbidity has been quoted as 50-60% with intact membranes (e.g. presenting with vaginal bleeding and fetal compromise) and 70-100% with ruptured membranes. Some caution needs to be expressed in considering these results since one reason for prenatally diagnosed cases as a group having a much better prognosis than those recognised after fetal exsanguination is potentially that tearing of aberrant vessels diagnosed prenatally might not occur in labour, and therefore the corollary that a prenatal diagnosis (if correct) might not lead to actual fetal haemorrhage in labour. In addition there is no firm way of establishing whether a prenatal diagnosis can reasonably be ratified at the time of delivery by planned caesarean section even though velamentous insertion can be identified on inspection of the placenta and membranes after delivery.	Two points arise; 1. In a true vasa praevia case – with vessels beneath the presenting part – it is highly unlikely that the vessels would not rupture during a vaginal delivery/labour. 2. Who would want to test this theory? VPRA do not believe that a woman advised of such a risk would seriously consider a vaginal birth. In respect of confirming the diagnosis after delivery this will depend entirely on the surgeon, obstetrican and/or midwife. Furthermore where vessels at or near the os which have been confirmed and re-confirmed by ultrasound are these really likely to have been wrongly diagnosed. – Cf what is the false positive rate for diagnosis of placenta praevia after abdominal delivery?
	A prenatal diagnosis followed by a planned caesarean section at 35 weeks of pregnancy (or earlier if there are signs of labour, significant bleeding occurs or the membranes rupture preterm) resulted in a 97% (59/61) survival compared to 44% (41/94) otherwise[5]. The authors felt that delivery at later gestational ages may negate the benefit of prenatal diagnosis. Others advocate delivery at 36 weeks again after a check on fetal lung maturity. In reality a threshold of 36-37 weeks in the absence of any other militating factors would also appear to be a reasonable approach under the circumstances, but there is no evidence as to the optimal time of delivery in cases of known vasa praevia other than a consensus that this should be once fetal maturity is reached. There is also the potential for maternal pressure to	The optimum time for delivery is entirely a matter for clinical judgment on a case by case basis – like any other pregnancy whether it is a high risk or a low risk pregnancy.

	influence earlier delivery.	
	The Apgar scores (a numerical assessment of the fetal condition at birth) of the survivors in cases not detected prenatally were low, averaging 1 at one minute and 4 at five minutes compared to 8 and 9 at one and five minutes respectively in those cases where a prenatal diagnosis had been made. Blood transfusion was required in 58% of neonates where a prenatal diagnosis has not been made, compared to 3% when diagnosed prenatally[5].	
	In an evaluation of pregnancy outcomes for women known to have vasa praevia compared to those without a prenatal diagnosis using a meta analysis of case reports, Fung & Lau[8] concluded that fetal loss rate and the incidence of neonatal transfusion were significantly less if the diagnosis was known before delivery.	
	Some authors[21] have advocated delivery by caesarean section in cases with "lower" velamentous cord insertion on the basis that this was analogous to vasa praevia and is associated with a very high rate of non-reassuring fetal status. Any impact on the caesarean section rate would be less if delivery by elective caesarean section were instead restricted to cases of prenatally diagnosed vasa praevia using colour Doppler.	The author and the NSC should consult Mr. Chris Griffin of Heart of England Foundation NHS Trust as he has strong views on the potential risks to the fetus by velamentous insertion.
	There has also been a suggestion that not all patients with vasa previa need to be delivered by caesarean section, with the example quoted being when there is a succenturiate lobe with small fetal vessels coursing near or over the cervix. Under these circumstances consideration of vaginal delivery with preparations for immediate intervention if necessary has been advocated instead. Nonetheless delivery by caesarean section would appear to be generally supported if fetal vessels are identified prenatally as coursing near or over the cervix. Compression of the vasa praevia by the presenting part resulting in decreased	This suggestion is not referenced, but it would be a brave obstetrican to attempt vaginal delivery in a type II vasa praevia case. Indeed the statement that the vaginal delivery should have a contingency for immediate surgery is we submit clear evidence of the lack of confidence in the suggestion. The last paragraph referring to compression should also refer to fetal distress.

	blood flow and possible fetal hypoxia has been postulated as a cause of fetal compromise.	
	A recent case report[31] has described successful in utero laser treatment of a Type II vasa praevia associated with a bilobed placenta despite subsequent spontaneous rupture of the membranes (whereas laser ablation of Type I vasa praevia would result in immediate fetal demise).	Whilst this is innovative and an exciting development for type II vasa praevia it is only relevant to type II and so far as VPRA are aware it has only been attempted once (but fortunately with a successful outcome).
	9. Evidence based policies covering who should be offered treatment and the appropriate treatment to be offered	
	There are no guidelines for the management of vasa praevia. From a practical point of view the prenatal identification of vasa praevia by the third trimester of pregnancy warrants the offer of delivery by planned caesarean section to avoid rupture of the fetal vessels and exsanguination. Prevention of perinatal mortality in this way is essentially intuitive and logical rather than based on any randomised trials.	There are known risk groups and known odds ratios for those groups – which should inform healthcare providers as to who they might selectively screen in the absence of guidelines. VPRA believe the time has come for guidelines to be issued. Suggested Guidelines can be found on our website; www.vasapraevia.co.uk – these have been adopted by several UK and overseas hospitals.
	10. Optimise clinical management and patient outcomes prior to screening	
	Ideally patient education and ultrasonography training are necessary prior to screening. The requirements for additional sonographer training are to be determined. Most units already offer a mid trimester ultrasound scan with equipment that incorporates Doppler flow facilities and include specific screening for other conditions such as isolated facial cleft (1:1000). There appear to be no ways of preventing vasa praevia from occurring prior to or during pregnancy.	VPRA has been told unequivocally that research funds are available included in the £1.7 billion set aside by the Government for "health service research". If those sonographers who do not possess the skills to make the diagnosis make themselves known, then funds and access to materials can be provided both by Government and VPRA (a registered charity). We have commissioned definitive educational presentations and training materials freely available via TheFetus.net (see above) which were specifically created to provide all the education required to make the diagnosis – and include how to avoid pitfalls. The presentations are available in over 12 languages.
	The Screening Programme	
	11 Evidence from high quality RCTs	

	that the screening programme is effective in reducing mortality or morbidity	
	There are no large prospective studies relating to vasa praevia and there is probably no place for a randomised controlled trial to investigate whether screening for vasa praevia would decrease fetal mortality, as it would be ethically unjustifiable given the poor fetal prognosis. The potential advantages of antenatal diagnosis is based on a number of small series and case reports. However it would seem difficult to counter the premise that a substantial improvement in fetal outcome in affected cases would be reliant on appropriate prenatal detection. Options for screening include universal identification of umbilical cord insertion with transvaginal and/or third trimester scanning in cases with velamentous insertion of the cord, or else targeted identification of umbilical cord insertion in cases known to be at increased risk of vasa praevia. Evidence on the efficacy of screening for velamentous insertion and vasa praevia has been explored above.	It is interesting to note the author's view that there is; *"..probably no place for a randomised controlled trial to investigate whether screening for vasa praevia would decrease fetal mortality, as it would be ethically unjustifiable given the poor fetal prognosis..",* as this was, in part, the view expressed by VPRA above. As we have addressed above, if it is the NSC's position that a randomised control study would be useful - what proposal does it make to carry one out? What would be the design of such a study?, and what evidence does the NSC consider it would derive from any such study that it does not already know or have access to, especially when one considers the author's view herein that; *"..it would seem difficult to counter the premise that a substantial improvement in fetal outcome in affected cases would be reliant on appropriate prenatal detection.."* This view is based upon the plethora of sound retrospective studies, case reviews and reports, **ALL** of which report an almost 100% success rate upon antenatal diagnosis as opposed to the dismal outcome in the absence of antenatal diagnosis. The option favoured by VPRA is for routine screening as part of the anomaly scan. Is this what the author means by; *"universal identification of umbilical cord insertion"*. If not, what is meant by this? The author then suggests transvaginal scanning for those identified with velamentous insertion of the cord. The other option identified by the author is a more targeted approach to identify the cord insertion in recognised risk groups. Is the author suggesting that this should be carried out at the anomaly scan? This is not clear.

	12 Evidence that complete screening programme is acceptable to public and health professionals	
	There is no evidence for or against the complete screening programme being acceptable to the public and to health professionals.	Whilst this is true in the sense that there is no published view of medical health professionals, the NSC are referred to Mr. Chris Griffin who conducted a review of obstetric professionals attending the Fetal Medicine Foundation 6th World Congress in Fetal Medicine, Croatia 2007 – where following a presentation to congress by Dr. Philippe Jeanty MD. PhD, one of the world's leading fetal radiologists, the delegates overwhelmingly voted in favour of adopting universal screening for vasa praevia as part of their routine anomaly scans. The NSC are also aware that there is massive public support and interest for universal screening – evidenced by a petition signed by over 3,000 members of the public and medical professionals which was submitted to Downing Street. There have also been a number of questions asked in Parliament and of Ministers by members of the public and Members of the House of Commons. In response to one of the Parliamentary answers provided nearly 1,000 members of the public disputed the correctness of the response given by the Minister; http://www.theyworkforyou.com/wrans/?id=2008-02-25e.188233.h There was also a huge public response to the questions posed by VPRA to the Prime Minister and his response posted on the Ask the PM You Tube web site. Additionally VPRA's web site is visited on average over 1,000 times per month – which is clear evidence of public and professional interest in the condition.
	13 Benefits to outweigh harm	
	Other than for primary prevention of fetal death through earlier planned abdominal delivery, neonatal morbidity as a result of partial exsanguination can occur, with complications relating to anaemia, hypovolaemic shock and complications of	On the available evidence there are clear benefits which outweigh the "harm" quoted for example; 1. Improvement of survival rate from 44% (undiagnosed) to 97% (diagnosed) (Oyelese 2004, Fung and Lau 1998)

	blood transfusion.	2. Reduction of perinatal morbidity such as low Apgar score or anemia requiring blood transfusions. (Oyelese 2004, Fung and Lau 1998).
	Neonatal complications include those relating to iatrogenic preterm birth as a result of early delivery by caesarean section, and include respiratory distress syndrome and transient tachypnoea of the newborn. Extended newborn nursery admissions can be expected due to relatively minor complications of prematurity. Much of this can be avoided if planned caesarean section took place at 37-38 weeks of pregnancy subject to there be no vaginal bleeding, threatened preterm labour or evidence of fetal compromise.	As above VPRA do not attempt to make recommendations on clinical matters which should be decided on a case by case basis with informed consent. What is clear is that the avoidance of fetal/neonatal death must be at the forefront of any decision making process.
	14 Opportunity cost economically balanced in relation to medical care as a whole	
	The cost of a national screening programme in the United Kingdom based on additional identification of umbilical cord insertion in the antenatal period has not been estimated.	VPRA have been advised by QCCH amongst others that including screening for vasa praevia within the anomaly scan has added little in terms of time or cost and they have continued to provide the anomaly scan within a 20 minute appointment. If cases are not diagnosed there are disproportionate and extra burdens placed on the health service; i.e. psychological trauma to parents (counselling and/or treatment for); treatment of resuscitated neo-nates; ongoing healthcare expenses for compromised survivors (not including those whose parents may litigate) – in respect of medical care as a whole these costs are likely to far outweigh the costs of screening for the condition.
	15 Plan for managing and monitoring the screening programme with an agreed set of quality assurance standards	
	In the absence of national screening in the United Kingdom, no quality assurance standards have been agreed.	This would be easily done by following the models set up at, inter alia, QCCH.
	16 Adequate staffing and facilities available	

	Colour Doppler is not currently employed during the course of the routine fetal anomaly scan. Additional time would be required for identifying the umbilical cord insertion and for performing an initial colour Doppler scan followed by an additional transvaginal scan where indicated. Whereas in theory this can be accomplished relatively quickly there is a need to consider the extent to which time is spent looking through the prescribed menu of fetal abnormalities and in the context of the wider ultrasound service. In addition there would be a need to explain the procedure to the patient, obtain verbal consent and prepare patients for a vaginal scan if they agreed to this extra investigation. Proponents of screening argue that no additional skills or training would be required by those performing the fetal anomaly scan although this would need to be confirmed at a practical level in day to day practice. All ultrasound scan machines employed for fetal anomaly scans should already have the required specification for vasa praevia screening and incorporate a colour flow Doppler facility. The RCOG advises that all ultrasound equipment for obstetric use should be less than five years old.	The first sentence is not agreed, though it is accepted that whilst grey scale is the common medium, colour Doppler is frequently used during routine anomaly scans – i.e. assessing fetal heart structure and blood flow etc. VPRA believe that all the necessary equipment exists within the NHS and that no additional skills or training would be required by sonographers who are competent to perform the anomaly scan. As above VPRA would be willing to provide assistance and training for any sonographer who believes it necessary. Though any sonographer who is competent to conduct the anomaly scan should be competent to make the diagnosis of vasa praevia. Whilst VPRA firmly believe that all sonographers ought to possess the necessary skills, the Government have set aside funds for medical research to include research into vasa praevia and this could be used to establish whether such training would be necessary.
	Nomiyama et al (1998)[20] instructed a single sonographer to take additional time and image the placental cord insertion in 587 cases. The mean time required for the examination was 20 seconds and in 95% of the cases the cord insertion was diagnosed within 1 minute (the assessment being limited to a maximum of 2 minutes). Sepulveda et al[6] were able to complete the assessment in less than 1 minute in 95% of cases.	QCCH amongst others have also found this and they continue to provide routine anomaly scans within a 20 minute appointment – which includes assessment of cord insertion and a flash of colour Doppler over the internal os. Daly Jones et al; "..the aim of this paper is to persuade all those undertaking the detailed anomaly scan that excluding vasa praevia is a worthwhile endeavour and one that is easily achievable within the confines of the second trimester scan.."
	Studies on cord insertion in the first trimester have variously limited the time allocation for this aspect of the scan to 1-5 minutes, with the mean time required to locate the cord insertion site with a time limit of 1 minute being 13.5 seconds. In a personal series Sepulveda[16] estimated that	Given the foregoing why does the author believe, without recourse to any evidence, that the timescale is unlikely to be replicated in the context of a universal screening program? The author accepts that NHS hospital must possess the right equipment, and having addressed training

	visualisation of the umbilical cord insertion was successfully achieved in all cases adding less than 30 seconds to the overall time allocated to the scan. This timescale is unlikely to be replicated in the context of a universal screening programme.	requirements (where necessary) VPRA believe that the majority of cases could be screened for umbilical cord insertion and a flash of colour Doppler over the internal os in under one minute. "..the method for excluding vasa praevia is a simple colour Doppler technique, and uses skills that trained practitioners already possess and takes approximately a minute of extra examination time. Vasa praevia is life threatening to a healthy baby: a proper diagnosis and an elective caesarean section easily prevent death.." Daly Jones et al.
	17 Other options for managing the condition	
	Digital palpation of fetal vessels within the membranes, amnioscopy before amniotomy, fetal blood detection testing and MR scanning are not viable alternatives to early diagnosis and preventative actions. Detection of aberrant vessels using digital palpation or amnioscopy may be difficult to effect and can precipitate haemorrhage. The risk of an adverse perinatal outcome once the cervix has dilated means that diagnosis prior to labour is optimal. Chemical tests to evaluate fetal bleeding for vasa previa can be simple and are potentially useful in the acute emergency situation[32]. By then however the fetal prognosis will remain poor with fetal haemorrhage. Prenatal screening and diagnosis using ultrasonography appears to be the least invasive and is an approach that can be used universally.	Of all the options discussed, VPRA are pleased to note that author accepts that ultrasound is the least invasive method of making the diagnosis and can be used universally.
	<u>Placenta Praevia Update:-</u>	
	Placenta praevia is responsible for potential life-threatening haemorrhage, both antenatally and intrapartum. The prevalence of clinically evident placenta praevia is estimated at 2.8/1000 singleton pregnancies and 3.9/1000 twin pregnancies. Perinatal mortality rates are 3-4 times higher than in normal pregnancies. Currently the placental site is routinely reported at the time of the mid-trimester ultrasound scan and this is the main screening test for placenta praevia. There is an acknowledgement that despite	

	the established routine use of ultrasound to diagnose placenta praevia, evidence-based classification and strategies have failed to evolve over the years. Low lying placenta is a shared risk factor for diagnosing vasa praevia. The midtrimester scan significantly over-estimates the prevalence of placenta praevia (1:10), with most women progressing to an additional scan in the third trimester which shows that the placenta is no longer low-lying. Recent reports suggest limiting these third trimester scans to cases where the placental edge either reaches or overlaps the cervical os at 20-23 weeks of pregnancy. If the placental edge was more than 2 cm from the internal cervical os migration of the placenta always occurred (if less than 2 cm from the cervical os placental migration occurred in 88.5% of cases). Placental migration is less likely if the placenta is posterior or of there has been a previous caesarean section. Recent work has explored the role that measurement of the angle of the lower placental edge might have in reducing the false positive rate.	
	Given previous NICE and RCOG guidelines issued on this topic, the literature review has been restricted to published papers from the time of issue of the RCOG Guideline, and effectively between 2004-2008.	
	NICE Guidelines The NICE guidelines issued in 2008 advise that only women whose placenta extends over the internal cervical os at the time of the fetal anomaly scan should be offered another transabdominal scan at 32 weeks. If the transabdominal scan is unclear a vaginal scan should be offered. The guidance acknowledges that the transvaginal ultrasound is superior to trans-abdominal ultrasound in defining the relationship between the placental edge and the cervical os. However the relation ship between the edge of the placenta and the internal os changes as the pregnancy	

	progresses. The earlier the scan is carried out, the greater the prevalence of placenta praevia.	
	RCOG Guidelines The current (but older) RCOG guideline revised in October 2005 refers to transvaginal ultrasound being safe in the presence of placenta praevia and is more accurate than transabdominal ultrasound in locating the placenta. These guidelines were based on a literature search to 2004. The guidelines also advise it to be a reasonable antenatal imaging policy to perform a transvaginal ultrasound scan on all women in whom a low-lying placenta is suspected from their transabdominal anomaly scan (at approximately 20-24 weeks) to reduce the number of those for whom follow up will be needed". The guideline recommends that a further transvaginal scan is required for all women whose placenta reaches or overlaps the cervical os at their anomaly scan with those at risk of minor placenta praevia having this confirmed or excluded by transvaginal ultrasound at 36 weeks and those with major placenta praevia at 32 weeks. The existing guidelines advise antenatal imaging by colour flow Doppler ultrasonography in women who are at increased risk of placenta accreta (morbid adherence) but make no mention of vasa praevia. The subsequent shift in advice for the repeat scan from 36 to 32 weeks reflected the perceived need for increased awareness in the context of the risk of antepartum haemorrhage. **SOGC Guideline** A more recent guideline was issued on behalf of the Society of Obstetricians and Gynaecologists in Canada in March 2007[34]. The authors concentrate on the proven benefit in the use of transvaginal scanning for diagnosing and managing placenta praevia with its increased prognostic value rendering the imprecise terminology of the traditional classification obsolete. The	The failure to mention Vasa Praevia in the RCOG Guidelines has been noted by the author and should be addressed forthwith. It would appear to be inconsistent in its approach to the management of women at increased risk of APH and because the general prevalence of placenta accreta is less than that of vasa praevia.

	general shift in emphasis seen in more recent literature is to move to a system of reporting the actual distance from the placental edge to the internal cervical os at the time of the transvaginal scan. Management then will be influenced by the extent to which the placental edge reaches or overlaps the internal cervical os. Routine transabdominal scanning is associated with a false positive rate for the diagnosis of placenta praevia of up to 25%. A reclassification of placental position can occur in 60% of women who undergo transvaginal scanning after an initial transabdominal scan. Transvaginal scanning (TVS) has a sensitivity of 87.5%, specificity of 98.8%, a positive predictive value of 93.3% and a negative predictive value of 97.6% "establishing TVS as the gold standard for the diagnosis of placenta previa". This indicates that TVS if available may be used to investigate placental location at any time in pregnancy when the placenta is thought to be low-lying. There has only been one randomised trial comparing transabdominal to transvaginal scanning which confirmed that the latter was more beneficial[35]. Insofar as the 18-24 scan is concerned the guideline advises that when the placental edge reaches or overlaps the cervical os on transvaginal scanning (which will be seen in 2-4% of cases) then a repeat scan for placental localisation is recommended in the third trimester. Of these less than 20% persist as placenta praevia, with the likelihood of placenta praevia being effectively zero when the placental edge reached but did not overlap the cervical os. The risk increased significantly beyond an overlap of 15 mm, and an overlap of >25 mm had a likelihood of placenta praevia at delivery of 40-100%. The timing of the scan will influence the incidence of the placental edge reaching or overlapping the internal os with this occurring in 42% of cases between 11-14 weeks of pregnancy. The later the scan is carried out the fewer the lower the prevalence of placenta praevia. The effect of placental migration as the pregnancy progresses is recognised with	

	this continuing into the third trimester. The paper makes no mention of any links between the diagnosis of placenta praevia and that of vasa praevia.	
	Comparison of four sonographic modalities (transabdominal, perineal, transvaginal and transrectal) has shown the diagnostic superiority of TVS in the diagnosis of placenta praevia compared to the abdominal and perineal views[36], with the transrectal approach proving "equivalent to the standard transvaginal approach in depiction quality and diagnostic safety". The latter option would not be a realistic alternative in UK practice.	
	A case control study[37] using the anomaly scan as a screening test for placenta praevia concluded that the second trimester transabdominal fetal anomaly scan is a useful screening test for placenta praevia. This was assessed using test characteristics of placental location at the mid trimester scan for identifying placenta praevia at term. The study showed that there was no benefit in the further testing of women with a placenta to os measurement greater than 2 cm at the midtrimester transabdominal scan. The authors recognised that TVS requires facilities and skills that might not be immediately available in all units and accepted that recall for later scans in pregnancy may create heightened anxiety, inconvenience and unnecessary lifestyle restrictions among the potentially large group of women given a diagnosis of a low-lying placenta at the time of the mid trimester ultrasound examination. Using a placenta-os measurement cut-off point of < 2cm all cases of placenta praevia should be identified but 11.1% of women would have false positive results. Given this high false positive result and the much larger population of women without placenta praevia, the authors estimated that 23 women would have to be followed up to confirm one true placenta praevia. In order to minimise the false positive rate the	

	authors advocate immediate evaluation with TVS in order to overcome the limitation of the high false positive rate using just transabdominal scanning.	
	Cho et al[38] prospectively evaluated women with low-lying placentas and found that the incidence of placental migration was significantly higher when the placenta was anterior as opposed to posterior, suggesting that anterior placenta praevia and low-lying placenta may migrate more often and faster than posterior placenta praevia. The latter are also visualised more poorly using transabdominal scanning and this study employed TVS.	
	A different perspective on the prediction of abnormal placentation had been postulated by Shukunami et al[39]. The authors looked at the relationship between the angle of the lower placental edge between 12-16 weeks of pregnancy and the presence of a low placenta at term. TVS was used to screen 2543 pregnancies on a prospective basis and the angle measured when the placenta was seen to cover the internal os. There were significantly fewer degrees of angle in the low placenta group than in the those without a low placenta. They found that using a 74^{o} cut-off the sensitivity of a low placenta at term was 100% (9/9) with a false positive rate of 23%, a positive predictive value of 20% and a negative predictive value of 100%. The latter would allow for the elimination of additional scans in later pregnancy, with the authors adding that their prediction method for placenta praevia augments those of the literature as a predictive tool. Additional work is needed before this approach can be considered further.	
	The risk of placenta praevia is increased in women who have undergone in vitro fertilisation, with a six-fold increase risk compared to natural conceptions[40]. The authors compared outcomes in consecutive pregnancies and concluded that it was reasonable to attribute the difference to the reproductive technology rather than to	If the NSC are to recommend counselling in relation to the risks of IVF it is clear that it would not provide women who have undergone IVF with all the information unless the risk of vasa praevia was also included within such counselling advice. Given this comment by the author;

	maternal factors, to the extent that women undergoing in vitro fertilisation should receive counselling in relation to these risks[41]. Assisted conception is therefore also a shared risk factor with vasa praevia. Ultrasound has a place in the diagnosis of vasa praevia especially in cases where the placental edge covers the os in mid-pregnancy but recedes later on. Lee et al[2] found that in 8 of the 18 cases of vasa praevia the placental edge was initially seen to be overlying the cervical os but later developed vasa praevia when the placental edge receded from the cervix. A retrospective case control study[42] has demonstrated that women with placenta praevia had an increased risk of velamentous cord insertion (7.5%), suggesting a shared aetiological pathway. This group also linked placenta praevia with a history of infertility problems. The potential for vasa praevia should therefore be borne in mind when performing follow up scans for placenta praevia, and on the basis of the available evidence it is advisable to identify the placental cord insertion site whenever a low placenta is discovered.	"..The potential for vasa praevia should therefore be borne in mind when performing follow up scans for placenta praevia, and on the basis of the available evidence it is advisable to identify the placental cord insertion site whenever a low placenta is discovered..." VPRA expect this to represent the minimum standard for all women whenever a low lying placenta is discovered. All such women must have the placental cord insertion site identified and a flash of colour Doppler over the internal os.
	Transvaginal scanning to ascertain risk of complications is a diagnostic option for both complications (placenta praevia and vasa praevia), with caesarean section being an intervention relevant to both.	VPRA agree however TVS is only an option where the diagnosis cannot be confirmed by TAS and with appropriate consent.
	Summary and Conclusions	
	(a) Vasa Praevia	
	1. Vasa praevia is a relatively rare condition with a high perinatal mortality which is seen more commonly in certain clinical circumstances (e.g. multiple pregnancies). Antenatal diagnosis is currently seldom made. Consideration could be given to inclusion of vasa praevia within the reporting framework of the UKOSS (United Kingdom Obstetric	VPRA would welcome the collection of data by UKOSS. It is essential if this is to be effective that awareness of the condition is increased amongst the medical profession so that occurrences of vasa praevia are correctly recorded. VPRA's website hosts clear ultrasound images and photographs diagrams of pathogical specimens which will aid such awareness. VPRA should stress however that we strongly believe that it would not be ethical to simply start

<table>
<tr><td></td><td>Surveillance System) as a mechanism of expanding the available data surrounding this condition.</td><td>collecting this data without also attempting to make the diagnosis antenatally.

UKOSS reporting should go hand in hand with antenatal screening – for obvious ethical reasons.</td></tr>
<tr><td></td><td>2. Complications arising from vasa praevia are an ongoing cause of perinatal mortality and morbidity. Measures to prevent and reduce perinatal mortality and morbidity are to be encouraged. The perinatal loss rate and the incidence of neonatal transfusion associated with vasa praevia are significantly less if the diagnosis is known before delivery.</td><td>VPRA agree. “..Measures to prevent and reduce perinatal mortality and morbidity are to be encourages..”. Universal screening for vasa praevia would without question reduce perinatal mortality in approximately 269 – 552 cases in the UK.

Additionally this is a clear acceptance of benefits outwirhing harm</td></tr>
<tr><td></td><td>3. Prenatal diagnosis will allow for abdominal delivery and prevention of fetal haemorrhage.</td><td>Agreed.</td></tr>
<tr><td></td><td>4. Vasa praevia has been variously reported as occurring in 0.015-0.04% of all pregnancies. The condition can be recognised prenatally using ultrasound by identifying cases where there is velamentous insertion of the umbilical cord and then screening these cases for vasa praevia.</td><td>Frequency of Type I and Type II of vasa previa.

<table><tr><th>Author</th><th>n</th><th>Type I</th><th>Type II</th></tr><tr><td>Devesa 1996</td><td>1</td><td>1</td><td>0</td></tr><tr><td>Oyelese 1998</td><td>3</td><td>2</td><td>1</td></tr><tr><td>Baschaat 1998</td><td>5</td><td>2</td><td>3</td></tr><tr><td>Fung and Lau 1998</td><td>3</td><td>3</td><td>0</td></tr><tr><td>Nomiyama 1998</td><td>1</td><td>1</td><td>0</td></tr><tr><td>Hertzberg 1998</td><td>2</td><td>0</td><td>2</td></tr><tr><td>Lee 2000</td><td>15</td><td>10</td><td>5</td></tr><tr><td>Catanzarite 2001</td><td>10</td><td>2</td><td>8</td></tr><tr><td>Hasegawa 2007</td><td>3</td><td>1</td><td>2</td></tr><tr><td>Baulies 2007</td><td>9</td><td>8</td><td>1</td></tr><tr><td>Total</td><td>52</td><td>30 (57.7%)</td><td>22 (42.3%)</td></tr></table>
According to the literature (see table above) about 60% of the vasa praevia are Type I and 40% Type II. If screening were limited to identifying cord insertion alone this would potentially miss the 40% of the vasa praevia.

Therefore, the correct strategy to screen for vasa praevia should be to carry out a short sweep with colour Doppler over the internal os, this would</td></tr>
</table>

		diagnose both types of vasa praevia. This should not be time consuming, as the assessment of the internal os should be part of the routine in screening for placenta praevia, and would simply require colour Doppler to exclude the presence of aberrant vessels in front of the cervix. The examination should be combined with a transvaginal scan in case of any doubt.
	5. Velamentous insertion occurs in approximately 1% of singleton pregnancies. Of these just 2% will be identified as having vasa praevia.	
	6. Placental cord insertion and velamentous cord insertion can be consistently identified with the help of transabdominal colour flow Doppler imaging at the time of the mid trimester fetal anomaly scan.	VPRA agree that this can be done and can see no contrary evidence in this review or elsewhere in the literature. In the circumstances universal screening for vasa praevia should be introduced into the midtrimester anomaly scan.
	7. The evidence indicates that failure to exclude a velamentous cord insertion or indeed vasa praevia as part of a screening programme should not be an indication to manage the pregnancy in any other way (i.e. assuming that there is a vasa praevia rather than the contrary). If on the other hand an ultrasound scan raises the possibility of vasa praevia then this should be reported in order to guide any additional ultrasound examinations in the third trimester.	Not only to guide any additional ultrasound examinations, but to enable the clinical team and the mother to agree on an appropriate management plan.
	8. The main systems to achieve such a screening process are in place (the provision of routine midtrimester fetal anomaly ultrasound scans and the ultrasound equipment required). The evidence suggests that relatively little in the way of extra scanning time might be required in the vast majority of women, but that some will require additional vaginal scans where	VPRA agree and we are pleased that the author; 1. Accepts that the main systems to achieve such a screening process are in place, and 2. The time for screening to be carried out is in during the routine midtrimester fetal anomaly ultrasound scan. 3. That the evidence suggests that relatively little in the way of extra scanning time might be required.

	none would otherwise have been indicated. Such resources would need to be evaluated in the context of a wider approach to screening for this condition. All of this would need to be factored into the costs of any universal screening programme. Potential staff education and training needs are yet to be identified and defined as necessary.	VPRA queries however what process is to be used to evaluate the resources needed if this is thought necessary and whether any steps are to be taken to evaluate education and training needs. VPRA have some resources and the Government have set aside resources for any staff education or training.
	9. There would appear to be a need to be a greater general awareness of the condition and of the potential for prenatal diagnosis.	VPRA welcome any attempts to raise awareness of this condition and the ability to diagnose it prenatally and would like to know what is proposed to further this? Since our formation, though there has been much hyperbole, there has been little evidence of the authorities taking positive steps to create such awareness.
	10. At face value universal screening is an attractive and desirable option in order to reduce perinatal mortality. However published evidence in relation to the wider ramifications of adopting this approach on a universal basis is limited and there is currently insufficient evidence to determine whether this might be a useful tool to incorporate into the fetal anomaly scan. There is insufficient evidence to base a decision to implement universal screening for velamentous insertion of the umbilical cord and vasa praevia on cost-effectiveness, with an emphasis on the human aspects of the problem, the potential to successfully recognise this prenatally, its relative rarity, potential ease of diagnosis and the avoidance of preventable perinatal deaths of otherwise healthy infants all needed to be taken into consideration.	VPRA accept the first sentence. VPRA question the ethics of a failure to introduce a universal screening program. If this is due to the fact that published prospective evidence is limited we repeat the question, if a randomised control study is required by NSC how do they propose to carry this out and when will it begin? What information would it provide that intuition and vast amounts of other published literature does not? VPRA are unclear as to how the author has come to these conclusions given his earlier statement that; *"..there is probably no place for a randomised controlled trial to investigate whether screening for vasa praevia would decrease fetal mortality, as it would be ethically unjustifiable given the poor fetal prognosis. The potential advantages of antenatal diagnosis is based on a number of small series and case reports. However it would seem difficult to counter the premise that a substantial improvement in fetal outcome in affected cases would be reliant on appropriate prenatal detection.."* With the above in mind it is difficult to envisage how a published prospective study or RCT, were it allowed, could provide any additional information

		for any proposed guidelines. The prevention of perinatal death of otherwise healthy infants is the paramount consideration. Other factors clearly in favour of universal screening include the author's acceptance that this can be easily diagnosed by ultrasound and that it can be successfully recognised prenatally. VPRA also query the issue of; "..cost effectiveness, with an emphasis on the human aspects of the problem.." – what is meant by this? As has been discussed above and has been seen in practice (QCCH) little will be added in terms of time and cost of the anomaly scan. Rarity is relative. There are literally umpteen conditions screened for which when discovered, provide little or no ability for the obstetrician or parent to intervene prior to delivery. VASA PRAEVIA is almost if not unique in as much as the antenatal diagnosis of the condition presents an opportunity to intervene and prevent the death or serious compromise of the baby.
	11. The potential effects on maternal anxiety, preterm delivery rates and incidence of caesarean section have not been evaluated and are important in the context of universal screening. This is desirable as part of the development of a screening programme for vasa praevia.	Dealing with maternal anxiety we refer to our observations above and add that of course the converse is true for undiagnosed cases and to properly evaluate maternal anxiety, one must consider the almost immeasurable psychological harm caused to parents in these cases; the attendant costs associated with dealing with such an emergency; and the neonatal unit costs in caring for those resuscitated neonates. Further the potential ongoing health care costs for severely compromised survivors are an important factor too. Dealing with caesarean section rates and prematurity rate; it is worthy of note that these factors have been suggested without any recourse to data at all. Given the apparent low prevalence of the condition, it is unlikely that the antenatal diagnosis of vasa praevia would have any impact on these rates. VPRA are confident that there is simply no data to contradict this statement, additionally where in the studies referred to herein

		there has been a "false positive" diagnosis at a midtrimester scan, the data suggests this has always led to a review of the diagnosis without recourse to obstetric surgical intervention, which points away from an impact on caesarean rates. Properly managed the resultant increase in Apgar scores for diagnosed as opposed to undiagnosed cases is clear evidence that there should be little concern about conditions associated with prematurity. Nonetheless Professor David Edwards Consultant Neonatologist QCCH has argued that he would; *"..rather deal with respiratory distress syndrome in a neo-nate than have to deal with multiple organ failure caused by fetal exsanguinations.."* However by the authors statement that this is desirable as part of the development of a screening programme for vasa praevia are we to take it that a screening programme has been devised?
	12. There is no agreed pathway for the obstetric management of prenatally diagnosed vasa praevia e.g. with regard to the timing of abdominal delivery. This is desirable in the context of the consequences of wider screening for vasa praevia.	*"..There is no agreed pathway for the obstetric management of prenatally diagnosed vasa praevia e.g. with regard to the timing of abdominal delivery.."* As a conclusion this is of course correct, however one wonders how any agreed pathway can really be devised beyond taking each case by case? There will be instances of vasa praevia with twins for example who are likely to be delivered much earlier than singletons. There will be women who have bled during pregnancy. There can be no fixed pathway, and so in VORA's estimation this has no real bearing in the context of antenatal screening – which is diagnostic – not management. In so far as management is concerned VPRA believe this should be a matter of individual clinical judgment, however suggestions have been made by commentators, i.e. Oyelese et al suggested "serial transvaginal cervical length determinations, along with hospitalization should the patient experience contractions or spotting, with a plan for elective delivery at about 35 weeks of gestation". This might be considered a good approach, and in asymptomatic women with a long cervix and properly monitored a caesarean section at 36-37

		weeks could be considered.
	13. In the absence of a universal screening programme, selective screening of cases with an increased risk of vasa praevia would be a useful mechanism to evaluate the screening process further and allow for prenatal diagnosis in cases of increased risk of this condition. These include multiple pregnancies, placenta praevia, placental variations (e.g. bilobed) and in vitro fertilisation. Initial selective screening would also allow for the introduction and dissemination of wider education and training. Outstanding issues relating to a wider programme screening can then be explored in greater detail prior to universal adoption.	The first sentence suggests that the author has concluded that selective screening is the minimum that must be introduced. VPRA would accept this as a mechanism to establish the validity of screening for vasa praevia, prior to universal routine screening for all. If we have understood this correctly could we please be advised as to when a selective screening program is to be rolled out and what form this will take? Are we correct in assuming that such selection will be based on women in the identified risk groups at the 20 week fetal anomaly scan? If this is proposed, how long is it envisaged that such a programme will run before further evaluation for a universal screening programme?
	14. Cases suitable for selective screening are those with a low-lying placenta in early pregnancy, those cases with succenturiate lobes, bilobed or multilobed placentas, multiple pregnancies and pregnancies that arise as a consequence of in vitro fertilisation.	VPRA agrees save that any such screening process would also have to build in a screening process for the detection of those cases with succenturiate lobes, bilobed or multilobed placentas.
	Placenta Praevia	
	1. Antenatal detection of placenta praevia is desirable in order to manage cases appropriately and reduce maternal and perinatal complications arising from this condition.	
	2. Placental localisation at the time of the fetal anomaly ultrasound scan is an established part of UK clinical practice.	
	3. The earlier a scan is carried out to look for placenta praevia, the higher the false positive rate compared to the prevalence of placenta praevia at term. The midtrimester scan overestimates	

	the prevalence of placenta praevia at term by 1:10, first trimester scans will demonstrate a placenta reaching or overlapping the internal os in as many as 42% of cases.	
	4. Additional work is required before conclusions can be reached on the merits of measurement of the angle of the lower placental edge in the first trimester of pregnancy in reducing the overall false positive rate.	
	5. A low-lying placenta is a shared risk factor for velamentous cord insertion and vasa praevia as is in vitro fertilisation.	
	6. The present NICE guideline concludes that women in whom the placenta extends over the internal cervical os at the time of the fetal anomaly scan should be offered another transabdominal scan at 32 weeks, with an additional transvaginal scan if there is still uncertainty.	VPRA query in the light of the author's findings whether the NICE guidelines will be amended to ensure that when screening at 32 weeks this scan will also seek to exclude the possibility of vasa praevia.
	7. The extent to which additional later scans are necessary could be reduced by the offer of a transvaginal scan at the time of the fetal anomaly scan in selected cases. There is insufficient evidence to draw reliable conclusions on the advantages and disadvantages of offering a transvaginal scan at the time of the routine fetal anomaly scan in selected cases as opposed to bringing women back for a repeat ultrasound examination in the third trimester. These factors would include practical issues of time allocation and patient considerations. 8. The timing of a confirmatory ultrasound scan in the third trimester has varied between 32-36	

	weeks depending on the extent of the placenta praevia. Although the shift from the RCOG guidance by NICE to 32 weeks for all women whose placenta extends over the os at the time of the fetal anomaly scan is based on a perceived need for awareness in the context of the risk of ante partum haemorrhage there does not appear to be strong evidence to demonstrate that this actually makes a difference to the management of asymptomatic patients.	
	9. The general shift in emphasis to reporting on the basis of actual distance from the placental edge to the cervical os (and the degree of overlap) as opposed to the adoption of a broader and more subjective classification is good practice which should be encouraged.	
	10. The evidence indicates that transvaginal scanning is the gold standard for the diagnosis of placenta praevia and is superior to transabdominal and transperineal approaches.	
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	Paul L Wood MD FRCOG ***1 November 2008***	