National Institute for Health and Care Excellence

IP1731 Bilateral cervicosacropexy or vaginosacropexy using mesh for pelvic organ prolapse

IPAC date: 12 December 2019

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	CONSENT ISSUES - WILL WOMEN BE COUNSELLED ON MESH RISK ADEQUATELY. MAY WE SEE THE PIL Evidence on the safety and efficacy of bilateral cervicosacropexy or vaginosacropexy using mesh for pelvic organ prolapse is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research.	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include appropriate patient information and consent.
2	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	The procedure uses PVDF - will this be classes as mesh? will women be given information that this is a plastic based permanently implanted medical device? Will women be told about the multiple complications in the few small scale studies?	Thank you for your comment. Yes, PVDF is a plastic used to create surgical mesh and we have used the word mesh in the title. The procedure description also describes it as a mesh. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include appropriate patient information and consent.

				When this guidance is published, a note on the NICE website will make it clear that this procedure is subject to the 'high vigilance restriction', which will be consistent with other IP guidance on mesh procedures. This will state: '*In July 2018, the Government announced a period of 'high vigilance restriction' on the use of a group of procedures, including this procedure, to treat stress urinary incontinence and pelvic organ prolapse, in England. This followed a recommendation by Baroness Cumberlege, who is chairing an independent review of surgical mesh procedures and has heard from women and families affected by them. For details, see the letter from NHS England and NHS Improvement to trust medical directors. The high vigilance restriction period was extended in March 2019. In April 2019, we updated our guideline on urinary incontinence and pelvic organ prolapse and published patient decision aids to support people to make informed decisions about surgery for stress urinary incontinence, uterine prolapse and vaginal vault prolapse*.'
3	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	People getting experimented on by definition have to be ill , there is a line to be drawn when you're talking about a long-term condition, not a fatal condition in terms of risk. • Safety and efficacy are not proven.	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include

				appropriate patient information and consent.
4	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	• It is also unclear how this procedure addresses urinary incontinence, though this is one of the claims made in support of this procedure.	Thank you for your comment. The indication for this guidance is pelvic organ prolapse, but the committee acknowledges that it may also have an impact on urinary incontinence.
5	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	Risks of use of mesh, Success/ failure unknown, • Safety of PVDA unknown.	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include appropriate patient information and consent.
6	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	Anecdotal adverse events (known from experience): • Detachment of the mesh from the cervix causing failure • Mesh complications including erosion, exposure and infection. • Bowel injury, bladder injury Theoretical adverse events: • There will be mesh related complications which the research suggests are less with this type of mesh than for polypropylene. (Note: need to identify/analyse research?) • The other complications are the same as for sacrocolpopexy • higher risk of ureteric damage due to the blind passage of the trocars • Discitis, back pain	Thank you for your comment. The overview has been updated to include the anecdotal and theoretical adverse events reported by the professional experts.

			What are the potential harms of the procedure? • bowel injury and • major haemorrhage, • pain and failure Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?	
7	Consultee 1 On behalf of 'Sling the Mesh' Patient support group	General	The training of clinicians performing these procedures is uncertain. It is not clear whether it is being performed within the umbrella for new procedures i.e. adequate Governance, adequate counselling and consent, adequate training of clinicians and adequate reporting and audit of complications.	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include appropriate patient information and consent.
8	Consultee 2 Health Professional Germany	**1.1**	Regarding 1.1 Since the bony dimensions of the female small pelvis are nearly identical among women of different ethnicities, all patients received CESA or VASA tapes of defined lengths (according to the obstetrical pelvic diameters) and widths (8.8cm or 9.3cm in length and 0.4cm in width). Therefore, all patients have no prolapse (POP-Q stage 0) after CESA or VASA surgery. These data are based on the experience of more than 1000 patients operated on CESA or VASA at the University Hospital of Cologne, a tertiary referral center, in Germany.	Thank you for your comment. IPAC only considers efficacy outcomes from peer-reviewed publications.
9	Consultee 2 Health Professional Germany	**1.2**	Regarding 1.2 A randomized controlled trial should compare two nearly	Thank you for your comment.

			identical surgical procedures. The CESA and VASA surgeries are standardized (same length, width, and shape of tapes). They are placed along defined anatomical sites (uterosacral ligaments and level of S1 at the sacral vertebra). The established prolapse surgeries lack that kind of standardization. Therefore, evaluation of clinical outcome may be hampered by these differences.	Section 1.2 has been changed to state that further research should also include details of the technique being used.
10	Consultee 2 Health Professional Germany	**2.3**	Regarding 2.3 Depending on the presence of the uterus, a supracervical hysterectomy is performed in CESA and in case of vaginal vault a VASA is performed.	Thank you for your comment. The committee discussed this comment, but decided not to change the guidance.
11	Consultee 2 Health Professional Germany	**3.1**	Regarding 3.1 The following published literature is missing: Ludwig S, Becker I, Mallmann P, Jäger W Comparison of Solifenacin and Bilateral Apical Fixation in the Treatment of Mixed and Urgency Urinary Incontinence in Women: URGE 1 Study, A Randomized Clinical Trial. In Vivo. 2019 Nov-Dec;33(6):1949-1957. doi: 10.21873/invivo.11690. Cassis C, Mukhopadhyay S, Morris E Standardizing abdominal sacrocolpopexy for the treatment of apical prolapse: One year on. Int J Gynecol Obstet 2019; 147: 49-53. DOI: 10.1002/ijgo-12935 Ludwig S, Morgenstern B, Mallmann P, Jäger W Laparoscopic bilateral cervicosacropexy: introduction to a new	Thank you for your comment. Ludwig S et al. (2019) is focused on incontinence as the indication and only included patients with grade 0 or 1 prolapse. It has therefore not been included in the overview. Cassis C et al. (2019) was identified in the updated search and has been added to table 2 of the overview. The second Ludwig S et al. (2019) paper is a case report and is included in the appendix of the overview. Jager W et al (2016) was not identified in the original search. It has been added to table 2 of the overview.

			tunneling technique. Int Urogynecoll J. 2019 Jul;30(7):1215-1217. doi: 10.1007/s00192-019-03911-2. Epub 2019 Mar 8. Ludwig S, Stumm M, Neumann E, Becker I and Jäger W Surgical treatment of urgency urinary incontinence, OAB (WET), mixed urinary incontinence, and total incontinence by cervicosacropexy or vaginosacropexy. Gynecol Obstet 6:404, 2016. DOI: 10.4172/2161-0932.1000404 Jager W, Ludwig S, Stumm M and Mallmann P Standardized bilateral mesh supported uterosacral ligament replacement - cervico-sacropexy (CESA) and vagino-sacropexy (VASA) operations for female genital prolapse. Pelviperineology. 2016; 35: 17-21	
12	Consultee 2 Health Professional Germany	**3.2**	Regarding 3.2 We noted the resolution of urinary incontinence (urgency urinary incontinence, mixed urinary incontinence) in women operated on CESA or VASA. Therefore, two clinical randomized trials (clinical trial identifier NCT01737411: Surgical vs. medical Treatment of Urge Urinary Incontinence in Women; clinical trial identifier NCT01737918: Treatment of Urge Urinary Incontinence in Women After Failure of Cesa or Vasa) comparing surgery (CESA or VASA) against standard medical treatment were performed. Compared to pharmacological treatment, the surgical repair of the apical vaginal end restored urinary continence in significantly more patients (42% vs. 10%).	Thank you for your comment. NCT01737411 is the URGE-1 study, published by Ludwig et al. (2019), which focuses on incontinence as the indication rather than pelvic organ prolapse. NCT01737918 is a Phase 1/2 Study of the Effect of TOT or Solifenacin After Cesa or Vasa on Urge Urinary Incontinence.
13	Consultee 3 NHS Professional	**General**	1. Abdominal sacrocolpopexy was first described in 1957 by Lane and sacrocolpopexy – either open or laparoscopic – remains the gold standard management of vaginal vault prolapse. Bilateral sacrocolpopexy/sacrocervicopexy using pre-designed mesh (CESA/VASA) replaces the uterosacral	Thank you for your comment. We do not include evidence from animal studies.

			ligaments with alloplastic tapes which act to re-attach the cervix or the vaginal vault in a more anatomically correct fashion. The mesh used is made of PVDF. In murine models, polyvinylidene fluoride (PVDF) mesh has been shown to be less inflammatory than polypropylene mesh.	
14	Consultee 3 NHS Professional	**General**	2. Traditional sacrocolpopexy using polypropylene mesh uses the sacral vertebrae (S1) for posterior fixation; however, attachment at the level of S2 is more anatomical as the uterosacral ligaments are attached at S2/3/4. We have performed over 100 of these procedures in our unit since 2014 and can confirm that bleeding in presacral area is no greater than a traditional sacrocolpopexy. We had only two cases of presacral bleeding which was controlled with pressure and packing.	Thank you for your comment about your clinical experience of using this procedure.
15	Consultee 3 NHS Professional	**General**	3. We have also published one-year safety data (enclosed) and there was not a single case of injury to the sigmoid colon.	Thank you for your comment and enclosing the safety data. Cassis C et al. (2019) has been added to table 2 of the overview.
16	Consultee 3 NHS Professional	**General**	4. When compared to traditional sacrocolpopexy, the volume of mesh used in bilateral sacrocolpopexy/sacrocervicopexy is considerably small. This is in keeping with the FDA recommendation stated in 2011 that the amount of mesh used should be minimised for treating vaginal prolapse. The incidence of mesh erosion in our study has remained low and out of the first 100 cases, only one patient had vaginal mesh erosion. The reported incidence of mesh erosion following a traditional sacrocolpopexy remains low between 1% and 8% for both open and laparoscopic routes, varying with type of mesh used.	Thank you for your comment and the information about mesh erosion incidence.
17	Consultee 3 NHS Professional	**1.1**	5. Restricting the procedure to be performed only on research context will not allow units like ours to offer the procedure as to treat apical prolapse. We have found this technique to be both efficacious and safe. Although dissection on the left side is not a standard practice and is viewed by many as a potentially risky step, this has not proved to be the case in our experience. We	Thank you for your comment. The committee discussed this comment but decided not to change the guidance.

			believe this provides a good option for those with recurrent prolapse.	
18	Consultee 3 NHS Professional	**General**	6. It is important to highlight that at a time when mesh is highly scrutinised, the advantage of using a standardised procedure with smaller volume of mesh allows comparison of outcomes between various units in addition to the benefit of smaller volume of implant. 7. As with any surgical procedure whilst operator experience is vitally important, post procedure surveillance and maintaining a registry allows to detect any mesh related complications. Apart from maintaining a local database we obtained consent from patients to enter their details into BSUG database. 8. Proper governance arrangements should be in place so that both patients and clinicians benefit from such novel procedure. Performing this procedure only for research purpose as suggested by NICE in their draft recommendations undermines units who have a track record of demonstrating the safety profile with good outcomes. It is important we accumulate long term data by entering data in national registry(BSUG database), the draft recommendation should take account of this fact. References: Karabulut A, Simavli SA, Abban GM, et al. Tissue reaction to urogynecologic meshes: Effect of steroid soaking in two different mesh models. Int Urogynecol J. 2016;27:1583–1589. Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse. 2011. https ://www.fda.gov/media/ 81123/ download. http://www.iciq. net/ICIQ-VS.html. Accessed March 22, 2019.	Thank you for your comment. The current high vigilance scrutiny approach to the use of mesh states that procedures should be entered on to a registry and that all adverse events should be reported to MHRA. The committee discussed this comment but decided not to change the guidance.

			Urogynecologic Surgical Mesh Implants. https ://www.fda.gov/medical-devices/implants-and-prosthetics/urogynecologic-surgicalmesh-implants. Accessed April 02, 2019.	
19	Consultee 3 NHS Professional	**Overview**	Please note our recent publication with 12 months data, not included in your consultation document. C L I N I C A L A R T I C L E Standardizing abdominal sacrocolpopexy for the treatment of apical prolapse: One year on Gynaecology Department, Norfolk and Norwich University Hospital, Norwich, UK Int J Gynecol Obstet 2019; 1–5	Thank you for your comment and alerting us to the new paper. The Cassis C et al. (2019) paper has been added to table 2 of the overview.
20	Consultee 4 Company FEG Textiltechnik mbH	**General**	Since its inception by Lane in 1962, sacrocolpopexy has evolved considerably. One aspect concerns the location of the posterior fixation. In traditional sacrocolpopexy as originally devised by Lane et al., the posterior part of the mesh is attached to the sacral promontory. However, soon afterwards there were modifications of the attachment point in order to restore a more physiological vaginal axis by attachment at the level of S1-S2 , or S3-S4 . The points of attachment have since further evolved to include bilateral fixation at the S1-level, , , or bilateral attachment to the iliopectineal ligaments. These methods of attachment show improved efficacy or safety profiles, e.g. due to a less complicated operating field or a more natural vaginal axis. The bilateral sacrocolpopexy, as devised for the CESA/VASA products, replaces or reinforces the natural anatomical structure of the uterosacral ligaments, and was first introduced in early 2013 and is the most modern method utilising the least amount of mesh-material.	Thank you for your comment. The Cassis C et al. (2019) paper has been added to table 2 of the overview.

			There is a marked difference between the number of meshes actually used in surgery and peer-reviewed publication of the results of these operations. Therefore, we are very much in favour of establishing a well-maintained mandatory registry, which can contribute to rapid detection of non-reportable complications and therefore would be in the interest of the patients as well as the manufacturers. In light of the upcoming changes due to the MDR 2017/745, compilation of post-market clinical data is an integral part of monitoring a product´s safety and efficacy. Further to the publications discussed in the draft report there is another study , published after the literature review mentioned in the procedural overview report including 100 patients. Furthermore, we hold additional unpublished data, which were collected as part of the implementation of the MDR 2017/745. In combination with the published data in the NICE overview of cervicosacropexy/ vaginosacropexy there are clinical data for over 12 % of all CESA/VASA-products implanted. Regarding the high rates of de novo SUI mentioned in the procedural consultation document, it is well known that de novo SUI is a frequent occurrence after treatment of prolapse of the vaginal stump or uterus. In the majority of cases this is due to occult SUI being present preoperatively, but remaining asymptomatic due to the prolapse of the vaginal stump or uterus. It is possible to diagnose occult SUI by means of urodynamical testing but this is rarely done in a clinical setting. This effect is further illustrated by the high occurrence of de novo SUI after treatment of prolapse of the vaginal stump or uterus with a pessary. The rate of de novo SUI for this non-invasive intervention amounts to 24 %. For alternative treatments of prolapse of the vaginal stump or uterus, such as sacrospinous ligament fixation (SSL) the rate of de novo SUI ranges from 2-11 %, , for sacrocolpopexy (SCP) from 2-24 %.9,	

			We would like to comment on some of the specific points of the consultation document.	
21	Consultee 4 Company FEG Textiltechnik mbH	**1.1**	1.1 "inadequate in quantity and quality" Given the high percentage of clinical data, we consider the amount of data for this procedure to be adequate to statistically significantly demonstrate non-inferiority of our product's efficacy and safety when compared to the state of the art.	Thank you for your comment. The committee discussed this comment but decided not to change the guidance.
22	Consultee 4 Company FEG Textiltechnik mbH	**3.4**	3.4 While it is imaginable that damage to the sacral plexus veins or the sigmoid colon may occur during the procedure, there are no reports (neither in the literature, nor via anecdotal evidence as obtained by the post-market surveillance system) that this has actually happened with the CESA/VASA products.	Thank you for your comment. In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). The committee sometimes chooses to comment on these. Section 3.5 of the guidance has been changed to include the word 'potential'.
23	Consultee 5 British Society of Urogynaecology and Royal College of Obstetricians and Gynaecologists	**1.1**	Recommendations: We strongly agree this procedure should only be permitted within the context of research. In the current climate, it is difficult to see that this procedure would be adopted widely without evidence from RCTs comparing it to existing procedures for vault/uterine prolapse recommended by NICE.	Thank you for your comment. Consultee agrees with main recommendation.
24	Consultee 5 British Society of Urogynaecology and Royal College of Obstetricians and Gynaecologists	**Title**	• We would recommend that the title include the abbreviations for these procedures (CESA & VASA) as it has been confused with abdominal sacrocolpopexy and abdominal sacrocervicopexy.	Thank you for your comment. The abbreviations have been added to the title.
25	Consultee 5	**1.1**	• In the current climate we feel there is a need for more safety data on this mesh. Perhaps the use of explant analysis	Thank you for your comment.

	British Society of Urogynaecology and Royal College of Obstetricians and Gynaecologists		could provide more evidence of it being inert in women. We would therefore recommend more research into the use of PVDF in women for the treatment of prolapse and its specific biocompatibility within this role prior to its further use for this procedure.	The recommendations state that this procedure should only be done in the context of research. The committee considered this comment but decided not to make any additional changes to the guidance.
26	Consultee 5 British Society of Urogynaecology **and** Royal College of Obstetricians and Gynaecologists	**General**	• We would recommend that all criteria required within the High Vigilance Scrutiny period for mesh procedures should be fulfilled for these as well. These include: -Entry of procedure to a Registry -Reporting of adverse events to the MHRA -Adequate training of clinicians undertaking the procedure -Collection of outcome data for all domains of pelvic floor function including sexual function and pain -Adequate consent (making patients aware this is an experimental procedure). • We note that this is a procedure that is not widely performed in the UK. -The mesh material is not widely used and is not recommended for use for POP in the NICE guideline (polypropylene mesh is the recommended material) -Concomitant hysterectomy is associated with a higher risk of mesh exposure/extrusion and the data presented is not sufficient to assess the risk for this procedure -The timing of the introduction of a new mesh device to the UK is interesting given the concerns regarding mesh procedures.	Thank you for your comment. The committee fully supports the requirements of the high vigilance scrutiny approach. When this guidance is published, a note on the NICE website will make it clear that this procedure is subject to the 'high vigilance restriction', which will be consistent with other IP guidance on mesh procedures. This will state: '*In July 2018, the Government announced a period of 'high vigilance restriction' on the use of a group of procedures, including this procedure, to treat stress urinary incontinence and pelvic organ prolapse, in England. This followed a recommendation by Baroness Cumberlege, who is chairing an independent review of surgical mesh procedures and has heard from women and families affected by them. For details, see the letter from NHS England and NHS Improvement to trust medical directors. The high vigilance restriction period was extended in March 2019. In April 2019, we updated our guideline on urinary incontinence and pelvic organ prolapse and published patient decision aids to support people to make informed decisions about surgery for stress urinary*

				incontinence, uterine prolapse and vaginal vault prolapse.' The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee, which will include the requirement to report adverse events to the MHRA.
27	Consultee 5 British Society of Urogynaecology and Royal College of Obstetricians and Gynaecologists	**General**	Factual Inaccuracies • The Interventional procedure overview implies this is a procedure done just for prolapse however of the 5 case series on which this is based , 1 actually refer to this as a procedure exclusively for Overactive bladder (Jager 2012) and a further 3 used Overactive bladder in conjunction with prolapse as a criteria for surgery (Joukhadar 2015; Ludwig 2016; Rexhepi 2018). In fact the German studies refer to this more as a procedure for urgency incontinence than prolapse. Only the UK study (Rajshekhar 2016) refers to this procedure as indicated exclusively for prolapse. The Jager study should therefore be completely excluded from the analysis. It is also somewhat bizarre that all the German studies used urinary incontinence as the primary outcome measure. This would not be expected practice for a procedure designed to treat prolapse. Relevant Evidence • This IPG is based on 5 case series, 1 from the UK and 4 from Germany • Outcomes reported on 3 of the studies are very short term – 3 months (Rajshekhar), 4 months (Rexhepi) and 7 months (Joukhadar) follow up. 2 studies have medium term follow up – 16 months (Ludwig) and 22 months (Jager).	Thank you for your comment. Although Jager et al. (2012) focused on incontinence as the indication for treatment, it did not specifically exclude patients with prolapse; 2 patients had a grade 2 prolapse and 2 patients had a grade 3 prolapse. A committee comment has been added, noting that the procedure has been used to treat different types of prolapse and urinary incontinence.
28	Consultee 5 British Society of Urogynaecology	**General**	• As each study has different inclusion criteria, (degree of prolapse and presence of urinary incontinence) uses different outcome measures and follow up is short, it is difficult to draw	Thank you for your comment.

	and Royal College of Obstetricians and Gynaecologists		conclusions about the efficacy of the procedure. Follow up duration is too short to evaluate the risk of mesh extrusion, exposure or infection. It is also not possible to establish what proportion of patients would need further surgery for recurrence or mesh removal due to complications. • Intraoperative complications do not appear to be rare or minor in 3 of the studies and are not individually reported in 2 studies. Bladder injury (1), wound infection (2), wound dehiscence (1), obstructed defaecation (1), new onset of bowel symptoms (2), significant (>1.2 litre) bleeding from the sacral venous plexus (2), intraperitoneal haematoma requiring surgery (2), new onset stress incontinence (5) and lower abdominal pain requiring surgery (1) are all described in three of the studies (in 193 patients). These are procedural risks rather than specifically related to the mesh. • Of the 5 studies, authors of 3 had funding from industry and 2 did not report funding.	The committee considered this comment but decided not to change the guidance.
29	Consultee 6 NHS England Specialised Commissioning	**General**	NHS England's Specialised Services' specialised Women's Services Clinical Reference Group have considered NICE documents on Bilateral cervicosacropexy or vaginosacropexy using mesh for pelvic organ prolapse and supporting evidence from the rapid literature search and the initial comments from their specialist advisors. The group note that the evidence base for this procedure is particularly poor. There are only five case series in the literature - some with very small numbers. The largest series of 133 patients is now 7 years old and has not been superseded in that time with any studies of a higher evidence level. The group do not feel that the body of supporting data is sufficient to recommend these techniques. The group notes that the specialist advisors comments reveal that very few people in the UK are doing these procedures so there would need to be significant training (perhaps from overseas surgeons) before widespread use. The group felt the evidence suggest that these procedures would only be suitable for highly regulated and ethically approved research trials.	Thank you for your comment. The committee considered this comment but decided not to change the guidance.

			Consideration of evidence from HES data on urogynaecological procedure volumes and outcomes from the National clinical Intelligence Programme would enhance the guidance by ensuring accurate assessment of the number of patients receiving this intervention. We would also suggest long term outcome studies focused on UK based patients who have already undergone this procedure using the British Society of Urogynaecology's outcome measures should be recommended within the guidance.	